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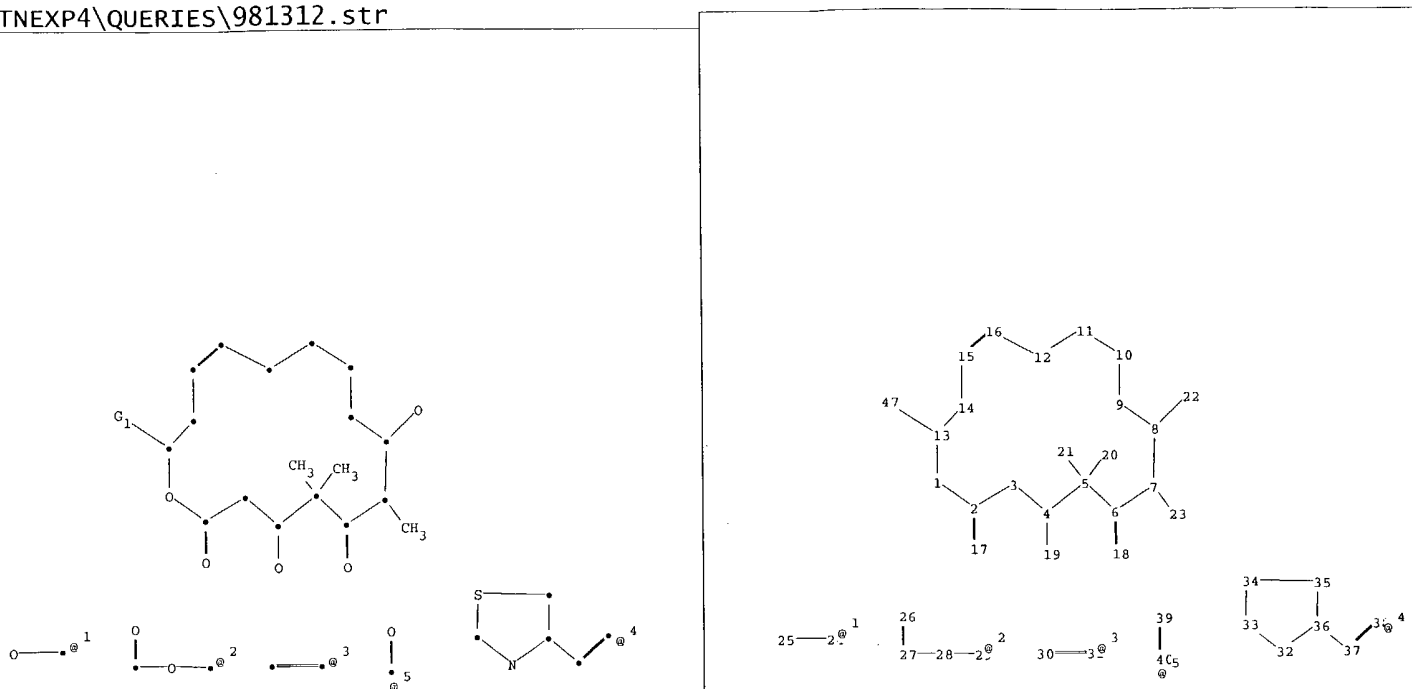

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2-17 4-19 5-20 5-21 6-18 7-23 8-22 13-47 24-25 26-27 27-28 28-29 30-31 36-37
37-38 39-40
ing bonds :
1-2 1-13 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-12 12-16 13-14 14-15
15-16 32-33 32-36 33-34 34-35 35-36
xact/norm bonds :
1-2 1-13 2-3 2-17 3-4 4-5 4-19 5-6 6-7 6-18 7-8 8-9 8-22 9-10 10-11 11-12
12-16 13-14 13-47 14-15 15-16 24-25 26-27 27-28 28-29 32-33 32-36 33-34 34-35
35-36 39-40
xact bonds :
5-20 5-21 7-23 30-31 36-37 37-38

1:[*1],[*2],[*3],[*4],[*5]

atch level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS 20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS
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39:CLASS 40:CLASS 47:CLASS

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=> d his

     (FILE 'HOME' ENTERED AT 15:29:43 ON 16 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 15:29:51 ON 16 JUN 2004
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L2              29 S L1
L3             485 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 15:30:58 ON 16 JUN 2004
L4             215 S L3
L5             131 S L4 AND PY<2002

=> d que l5 stat
L1             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L3             485 SEA FILE=REGISTRY SSS FUL L1
L4             215 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3
L5             131 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND PY<2002


=> d 1-131 ibib iabs hitstr
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L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:655116 CAPLUS
DOCUMENT NUMBER: 137:185358
TITLE: Preparation of epothilone analogs as anticancer agents
INVENTOR(S): Nicolaou, Kyriacos C.; He, Yun; Ninkovic, Sacha; Pastor, Joaquin; Roschangar, Frank; Sarabia, Francisco; Vallberg, Hans; Vourloumis, Dionisios; Winssinger, Nicolas; Yang, Zhen; King, N. Paul; Finlay, M. Ray
PATENT ASSIGNEE(S): The Scripps Research Institute, USA
SOURCE: U.S., 160 pp., Cont.-in-part of U. S. Ser. No. 856,533, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6441186	B1	20020827	US 1997-923869	19970904
WO 9825929	A1	19980618	WO 1997-EP7011	19971212 <--
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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AU 746597	B2	20020502		
EP 944634	A1	19990929	EP 1997-953808	19971212 <--
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CN 1246862	A	20000308	CN 1997-181771	19971212 <--
CN 1134443	B	20040114		
JP 2001504856	T2	20010410	JP 1998-526247	19971212 <--
US 6380394	B1	20020430	US 1998-102602	19980622

PRIORITY APPLN. INFO.: US 1996-32864P P 19961213
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OTHER SOURCE(S): MARPAT 137:185358
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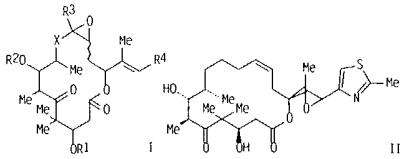

ABSTRACT:
Epothilone A, epothilone B, analogs of epothilone and libraries of epothilone analogs of formula I [R1, R2 = H, silyl group, Me, Ac, PhCO, tert-butoxycarbonyl; R3 = H, Me, CHO, (substituted) CO2H, etc.; R4 = heterocyclyl, etc.; X = (CH2)n; n = 1-5] are synthesized. Epothilone A and B are known anticancer agents that derive their anticancer activity by the prevention of mitosis through the induction and stabilization of microtubulin assembly. Several of the analogs are demonstrated to have a superior cytotoxic activities as compared to epothilone A or epothilone B as demonstrated by their enhanced ability to induce the polymerization and stabilization of microtubules. Thus, epothilones A and B are prepared via olefin metathesis and macrocyclization. II was prepared and showed 7% tubulin polymerization

IT **188259-95-2P 188260-34-6P 192370-82-4P**
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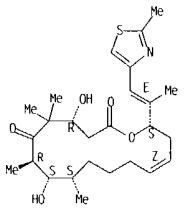
L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

209260-93-5P 209260-94-6P 209260-95-7P
209260-96-8P 209260-97-9P 209260-98-0P
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(prepn. of epothilone analogs as anticancer agents)

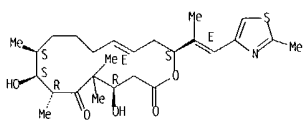
RN 188259-95-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-34-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

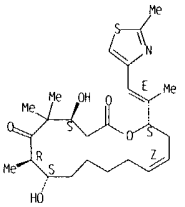


RN 192370-82-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Double bond geometry as shown.



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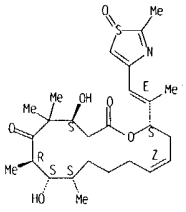
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-1-oxido-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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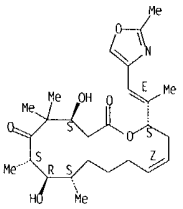
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-16-3 CAPLUS
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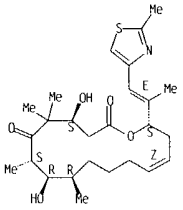
Absolute stereochemistry.
Double bond geometry as shown.



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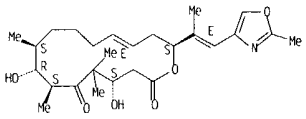
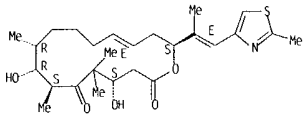
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-20-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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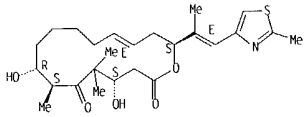
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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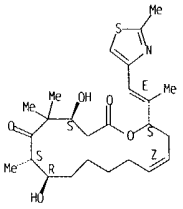
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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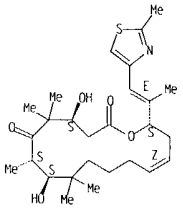
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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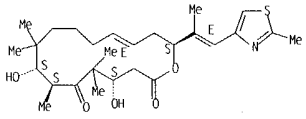
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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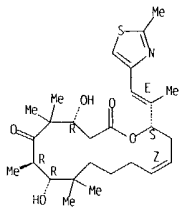
Absolute stereochemistry.
Double bond geometry as shown.



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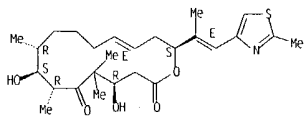
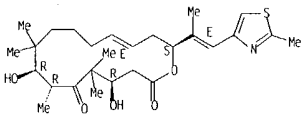
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-26-5 CAPLUS

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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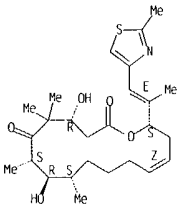
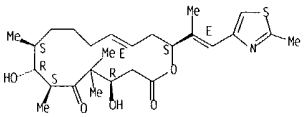
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-29-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9R,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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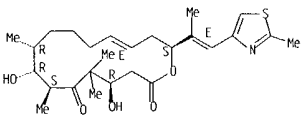
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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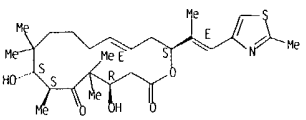
Absolute stereochemistry.
Double bond geometry as shown.



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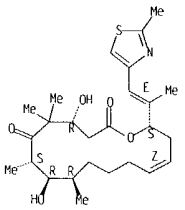
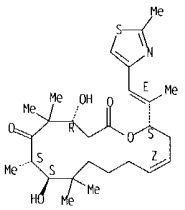
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-30-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8S,13Z,16S)-(9CI) (CA INDEX NAME)

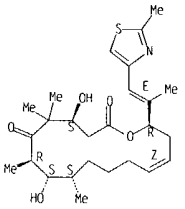
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-31-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

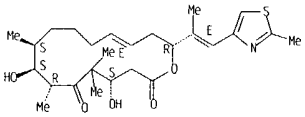
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



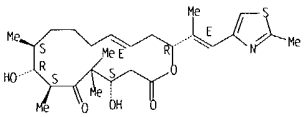
RN 198571-38-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-39-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16R)-(9CI) (CA INDEX NAME)

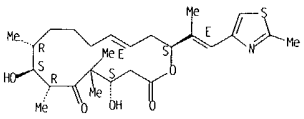
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-66-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-

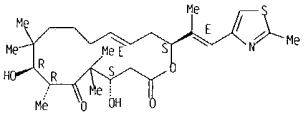
L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S,7R,8S,9R,13E,16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-67-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8R,13E,16S)-
(9CI) (CA INDEX NAME)

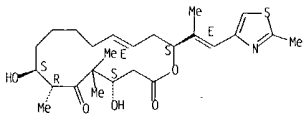
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-68-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-
methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13E,16S)- (9CI) (CA
INDEX NAME)

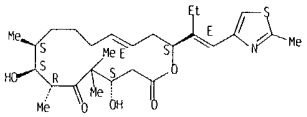
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-69-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-
[(1E)-1-[(2-methyl-4-thiazolyl)methylene]propyl]-, (4S,7R,8S,9S,13E,16S)-
(9CI) (CA INDEX NAME)

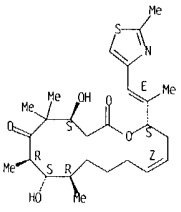
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-70-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13Z,16S)-
(9CI) (CA INDEX NAME)

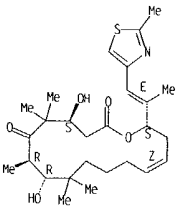
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-71-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8R,13Z,16S)-
(9CI) (CA INDEX NAME)

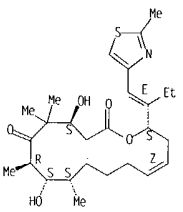
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-72-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-
[(1E)-1-[(2-methyl-4-thiazolyl)methylene]propyl]-, (4S,7R,8S,9S,13Z,16S)-
(9CI) (CA INDEX NAME)

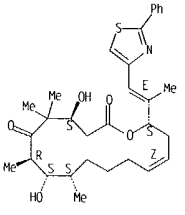
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-73-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-
[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-
(9CI) (CA INDEX NAME)

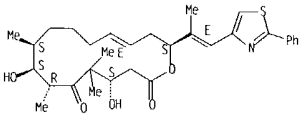
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-74-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-
[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-
(9CI) (CA INDEX NAME)

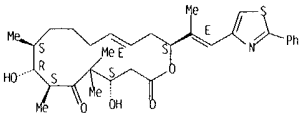
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-76-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

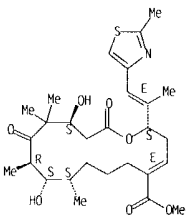
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-77-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

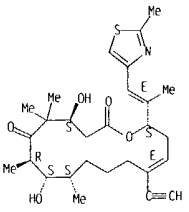
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-94-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethynyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

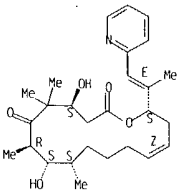
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 204513-12-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

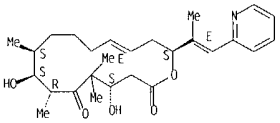
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-78-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

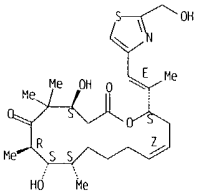
Absolute stereochemistry.
Double bond geometry as shown.



RN 201136-87-0 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxylic acid, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, methyl ester, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

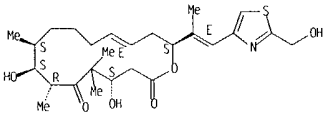
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-14-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

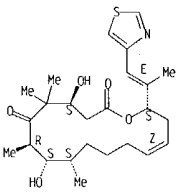
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

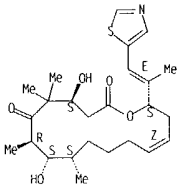
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-36-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

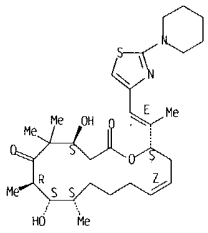
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-37-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

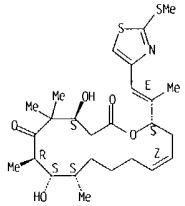
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-40-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

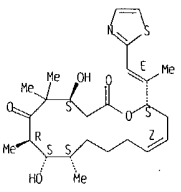
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-41-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

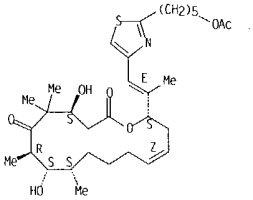
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-38-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[5-(acetyloxy)pentyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

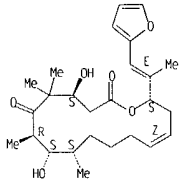
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-39-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(1-piperidinyl)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

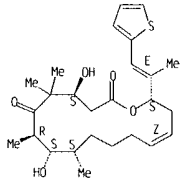
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-42-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

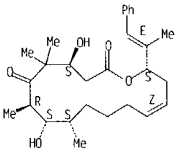
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-43-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

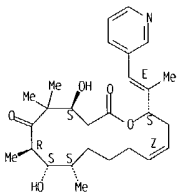
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-44-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

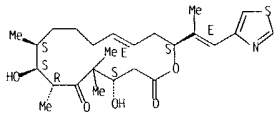
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-45-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

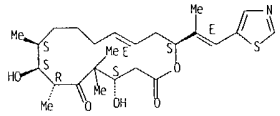
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



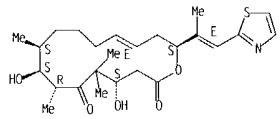
RN 204513-46-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-47-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

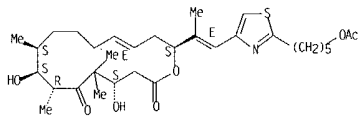
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-48-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[5-(acetyloxy)pentyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-.

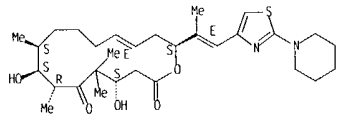
L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



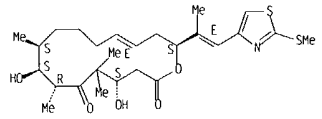
RN 204513-49-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(1-piperidinyl)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-50-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

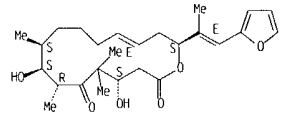
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-51-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA

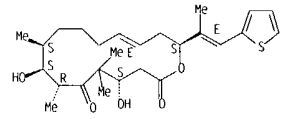
L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



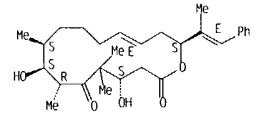
RN 204513-52-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-53-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

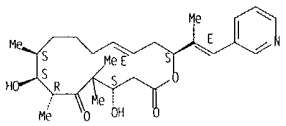
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-54-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA

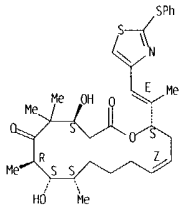
L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-87-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(phenylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

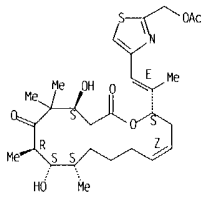
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-88-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethyl-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

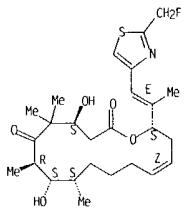
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 209260-91-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

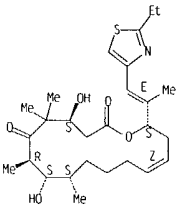
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-92-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(1-methyl-1H-imidazol-2-yl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

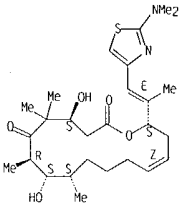
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 209260-89-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(dimethylamino)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

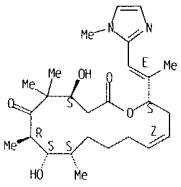
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-90-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[(acetyloxy)methyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

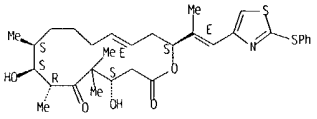
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



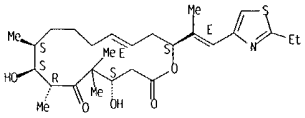
RN 209260-93-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(phenylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-94-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethyl-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

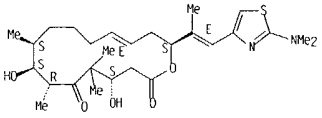
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-95-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(dimethylamino)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-,

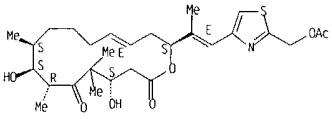
L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



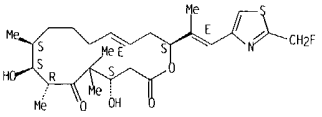
RN 209260-96-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[(acetyloxy)methyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

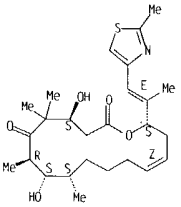


RN 209260-97-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

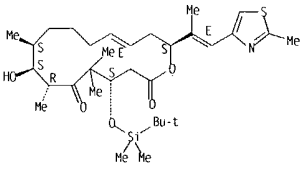


L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 187283-52-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



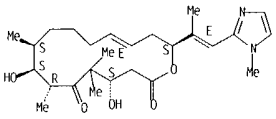
RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 209260-98-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(1-methyl-1H-imidazol-2-yl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

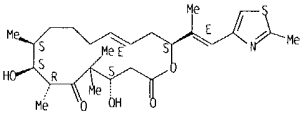
Absolute stereochemistry.
Double bond geometry as shown.



IT **186692-73-9P 187283-52-9P 188260-10-8P**
189453-10-9P 189453-40-5P 193071-86-2P
193146-35-9P 198475-12-6P 198571-09-4P
198571-10-7P 198571-11-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of epothilone analogs as anticancer agents)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

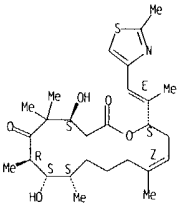
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



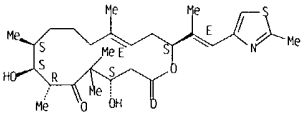
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

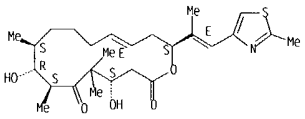
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 193071-86-2 CAPLUS

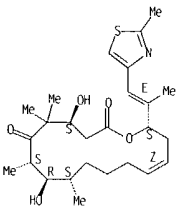
L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 193146-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

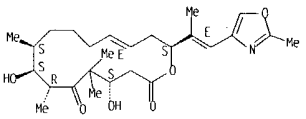
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198475-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

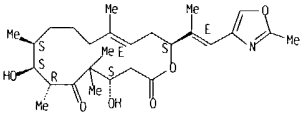
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-11-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

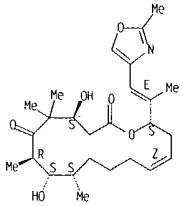
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **186692-84-2P 187283-49-4P 189453-35-8P**
190370-08-2P 193146-34-8P 198475-04-6P
201136-64-3P 201136-85-8P 201136-86-9P
201136-88-1P 202333-40-2P 202333-45-7P
203252-73-7P 203252-74-8P 204513-16-6P
204513-26-8P 204513-28-0P 204513-30-4P
209260-71-9P 209260-82-2P 209260-83-3P
209260-85-5P 209260-99-1P 209261-03-0P
209261-04-1P 209261-05-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilone analogs as anticancer agents)
RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

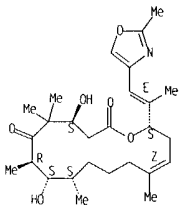
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-09-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

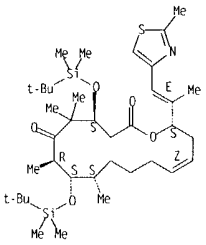
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-10-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

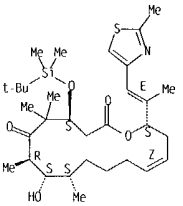
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 187283-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

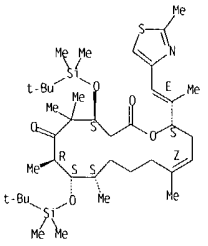
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

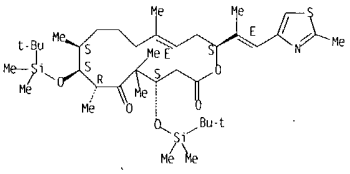
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 190370-08-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

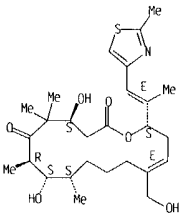
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 193146-34-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)- (9CI) (CA INDEX NAME)

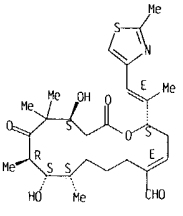
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-85-8 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxaldehyde, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

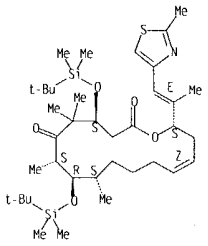
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-86-9 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxylic acid, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

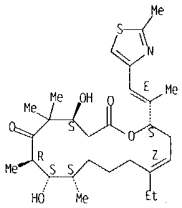
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-04-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

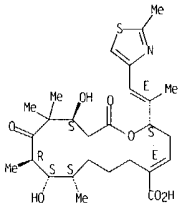
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-64-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

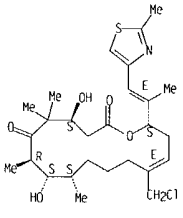
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-88-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(chloromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

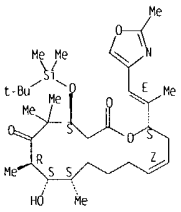
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 202333-40-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

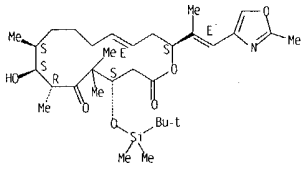
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 202333-45-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

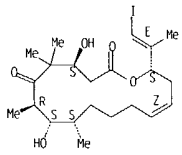
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 203252-73-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

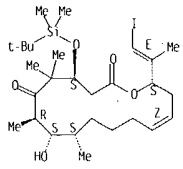
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



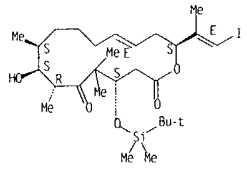
RN 204513-26-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

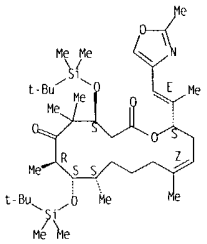


RN 204513-28-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

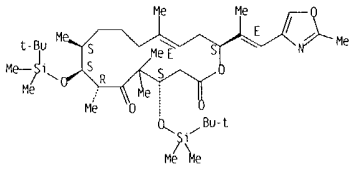


L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 203252-74-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

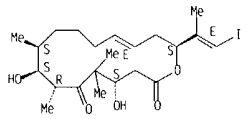


RN 204513-16-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

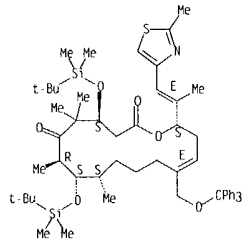
L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 204513-30-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-71-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-[(triphenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

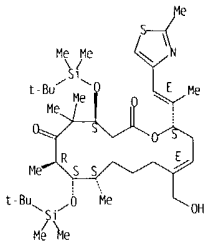
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 209260-82-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

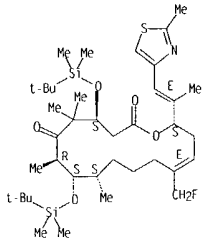
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



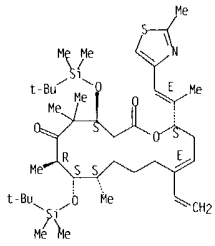
RN 209250-83-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(fluoromethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



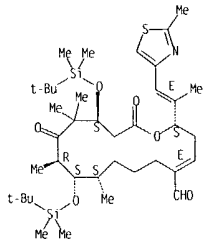
RN 209260-85-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(chloromethyl)-4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 209261-03-0 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxaldehyde, 10,14-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

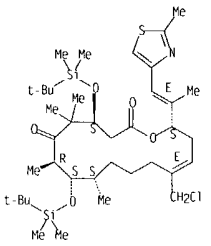


RN 209261-04-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-ethynyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

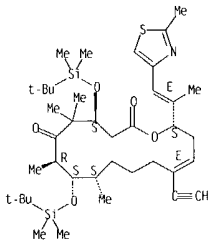
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 209260-99-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-ethenyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

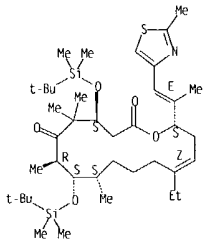
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 1 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 209261-05-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-ethyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

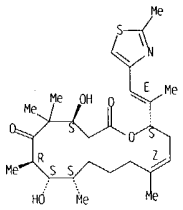
L5 ANSWER 2 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:484860 CAPLUS
DOCUMENT NUMBER: 137:62265
TITLE: Myxococcus host cells for the production of epothilones
INVENTOR(S): Julien, Bryan; Katz, Leonard; Khosla, Chaitan
PATENT ASSIGNEE(S): Kosan Biosciences, Inc., USA
SOURCE: U.S., 33 pp., Cont.-in-part of U.S. 6,303,342.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6410301	B1	20020625	US 2000-560367	20000428
WO 2000031247	A2	20000602	WO 1999-US27438	19991119 <--
WO 2000031247	A3	20001207		
W: AL, AM, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, IL, IS, JP, KG, KP, KR, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6303342	B1	20011016	US 1999-443501	19991119 <--
US 6583290	B1	20030624	US 2000-724882	20001128
WO 2001083800	A2	20011108	WO 2001-US13793	20010426 <--
WO 2001083800	C1	20030103		
WO 2001083800	A3	20030410		
WO 2001083800	C2	20030912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001095195	A5	20011112	AU 2001-95195	20010426 <--
EP 1320611	A2	20030625	EP 2001-973782	20010426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004508810	T2	20040325	JP 2001-580407	20010426
US 2003096381	A1	20030522	US 2002-191694	20020708

PRIORITY APPLN. INFO.: US 1998-109401P P 19981120

L5 ANSWER 2 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

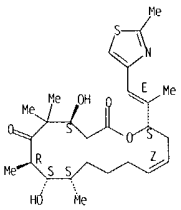
L5 ANSWER 2 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 1999-119386P	P	19990210	
US 1999-122620P	P	19990303	
US 1999-130560P	P	19990422	
US 1999-443501	A2	19991119	
WO 1999-US27438	A2	19991119	
US 2000-560367	A	20000428	
US 2000-232696P	P	20000914	
US 2000-257517P	P	20001221	
US 2001-269020P	P	20010213	
US 2001-825856	A	20010403	
US 2001-825876	A	20010403	
WO 2001-US13793	W	20010426	

ABSTRACT:
Recombinant Myxococcus host cell containing recombinant expression vectors containing epothilone polyketide synthase genes can produce epothilones C and D but not epothilones A and B.

IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(production of epothilones using recombinant Myxococcus host cells)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-

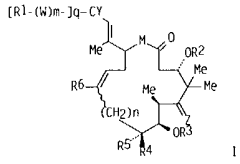
L5 ANSWER 3 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:368935 CAPLUS
DOCUMENT NUMBER: 136:385973
TITLE: Synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug resistant phenotype
INVENTOR(S): Danishefsky, Samuel J.; Stachel, Shawn J.; Lee, Chul Bom; Chappell, Mark D.; Chou, Ting-chao; Wu, Zhicai
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 125 pp., Cont.-in-part of U.S. Ser. No. 257,072.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002058286	A1	20020516	US 2001-797027	20010301
US 6204388	B1	20010320	US 1999-257072	19990224 <--

PRIORITY APPLN. INFO.:

US 1999-257072	A2	19990224
US 1996-32282P	P	19961203
US 1997-33767P	P	19970114
US 1997-47566P	P	19970522
US 1997-47941P	P	19970529
US 1997-55533P	P	19970813
US 1997-986025	A2	19971203
US 1998-75947P	P	19980225
US 1998-92319P	P	19980709
US 1998-97733P	P	19980824

OTHER SOURCE(S): MARPAT 136:385973
GRAPHIC IMAGE:



I

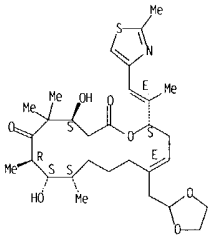
ABSTRACT:
The present invention provides convergent processes for preparing epothilones, desoxyepothilones, and analogs, e.g., I [M = NH, O; CY = aryl, heteroaryl; q = 1-5; W = absent, NH, CO, CS, O, S, C(V)2; V = H, halogen, OH, SH, amino,

L5 ANSWER 3 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(un)substituted alkyl, heteroalkyl, aryl, heteroaryl; m = 1-5; W-R1 = single bond, double bond; R1 = H, OR, SR, NR2; CO2R, COR, CONHR, N3, N2, N2R; halogen, un(substituted) cyclic or acyclic aliph., heteroaliph., aryl or heteroaryl, polymer, carbohydrate; R = H, un(substituted) cyclic or acyclic aliph., heteroaliph., aryl or heteroaryl, protecting group; R2, R3 = H, un(substituted) aliph., heteroaliph., aryl, heteroaryl, acyl, aroyl, benzoyl; R4, R5 = H, un(substituted) cyclic or acyclic aliph., heteroaliph., aryl or heteroaryl, optionally substituted by one or more of OH, alkoxy, carboxy, carboxaldehyde, N-alkoxyimino, N-alkoxyimino; R6 = H, OR, SR, NR2; CO2R, COR, CONHR, N3, N2, N2R, cyclic acetal, halogen, un(substituted) cyclic or acyclic aliph., aryl, heteroaryl; Z = O, N(ORE), NNRFRG; RE, RF, RG = un(substituted) cyclic or acyclic aliph.; n = 0-3], for the treatment of cancer. Biol. activities of novel compds. based on I and methods for the treatment of cancer and cancer which has developed a multi-drug phenotype are presented. Thus, desoxyepothilone B and desoxyepothilone F were active vs leukemia CCRF-CEM cells (IC50 = 0.095 μM; IC50 = 0.027 μM, resp.).

IT **198475-07-9P 252981-50-3P**, (-)-12,13-Desoxyepothilone F
350493-50-4P 359417-21-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilones, intermediates and analogs for use in treatment of cancers with multidrug resistant phenotype)

RN 198475-07-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(1,3-dioxolan-2-ylmethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

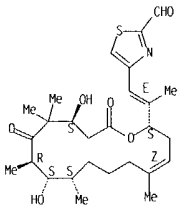
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 3 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 359417-21-3 CAPLUS
CN 2-Thiazolecarboxaldehyde, 4-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-10,14-dihydroxy-5,9,11,13,13-pentamethyl-12,16-dioxooxacyclohexadec-4-en-2-yl]-1-propenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **298702-21-3P 298702-22-4P 359014-38-3P**
359014-39-4P 359014-40-7P 359014-45-2P
426206-48-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilones, intermediates and analogs for use in treatment of cancers with multidrug resistant phenotype)

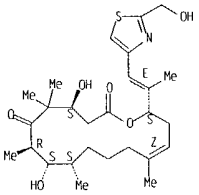
RN 298702-21-3 CAPLUS
CN Carbonic acid, [4-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-5,9,11,13,13-pentamethyl-12,16-dioxo-10-[[(2,2,2-trichloroethoxy)carbonyl]oxy]-14-[(triethylsilyl)oxy]oxacyclohexadec-4-en-2-yl]-1-propenyl]-2-thiazolyl]methyl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

L5 ANSWER 3 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

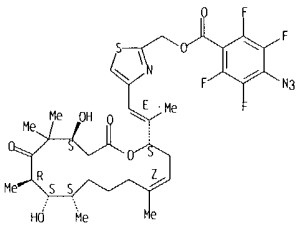
RN 252981-50-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

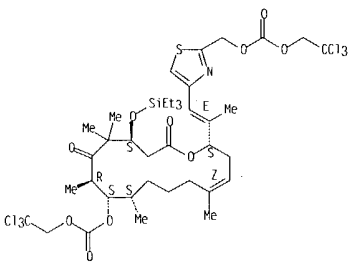


RN 350493-50-4 CAPLUS
CN Benzoic acid, 4-azido-2,3,5,6-tetrafluoro-, [4-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-10,14-dihydroxy-5,9,11,13,13-pentamethyl-12,16-dioxooxacyclohexadec-4-en-2-yl]-1-propenyl]-2-thiazolyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

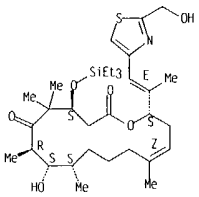


L5 ANSWER 3 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 298702-22-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-4-[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

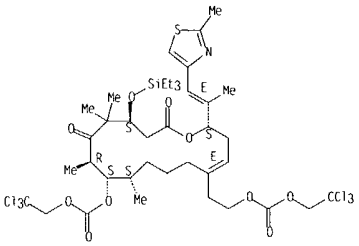
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 359014-38-3 CAPLUS
CN Carbonic acid, (4S,7R,8S,9S,13E,16S)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-2,6-dioxo-13-[2-[[(2,2,2-trichloroethoxy)carbonyl]oxy]ethyl]-4-[(triethylsilyl)oxy]oxacyclohexadec-13-en-8-yl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

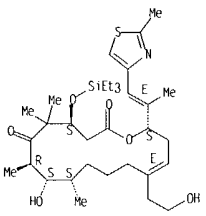
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 3 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 359014-39-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-13-(2-hydroxyethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

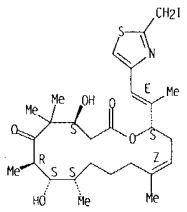
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



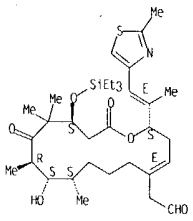
RN 359014-40-7 CAPLUS
CN Oxacyclohexadec-4-ene-5-acetaldehyde, 10-hydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-14-[(triethylsilyl)oxy]-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 3 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

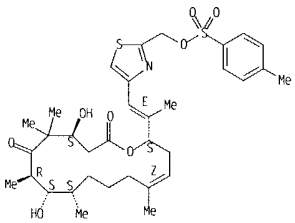


L5 ANSWER 3 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 359014-45-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-[2-[[[(4-methylphenyl)sulfonyl]oxy]methyl]-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 426206-48-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(iodomethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 4 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:332627 CAPLUS
DOCUMENT NUMBER: 136:340539
TITLE: Preparation of bio-intermediates for use in the chemical synthesis of polyketides via fermentation using recombinant polyketide synthase
INVENTOR(S): Santi, Daniel; Ashley, Gary; Myles, David C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 69 pp., Cont.-in-part of U.S. Ser. No. 867,845.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

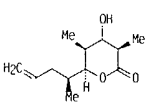
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002052028	A1	20020502	US 2001-927559	20010809
WO 2001092991	A2	20011206	WO 2001-US17352	20010529 <--
WO 2001092991	A3	20020808		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2004018598	A1	20040129	US 2003-441787	20030519

PRIORITY APPLN. INFO.:
US 2000-224038P P 20000809
US 2000-237382P P 20001004
US 2000-248387P P 20001113
US 2001-867845 A2 20010529
US 2000-207331P P 20000530
WO 2001-US17352 A 20010529
US 2001-927559 A3 20010809

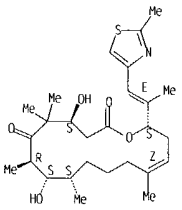
OTHER SOURCE(S): MARPAT 136:340539
GRAPHIC IMAGE:



L5 ANSWER 4 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
ABSTRACT:
The present invention relates to compds.. e.g. I. made by a subset of modules from one or more polyketide synthase ("PKS") genes that are used as starting material in the chemical synthesis of novel mols.. particularly naturally occurring polyketides or derivs. thereof. The biol. derived intermediates ("bio-intermediates") generally represent particularly difficult compds. to synthesize using traditional chemical approaches due to one or more stereocenters. In one aspect of the invention. an intermediate in the synthesis of epothilone is provided that feeds into the synthetic protocol of Danishefsky and co-workers. In another aspect of the invention. intermediates in the synthesis of discodermolide are provided that feed into the synthetic protocol of Smith and co-workers. By taking advantage of the inherent stereochem. specificity of biol. processes. the syntheses of key intermediates and thus the overall syntheses of compds. like epothilone and discodermolide are greatly simplified.

IT **189453-10-9P**. Epothilone D
RL: BMF (Bioindustrial manufacture): BPN (Biosynthetic preparation): IMF (Industrial manufacture): SPN (Synthetic preparation): BIOL (Biological study): PREP (Preparation)
(preparation of polyketides via fermentation using recombinant polyketide synthase)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9.13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13Z.16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:327944 CAPLUS
DOCUMENT NUMBER: 136:340536
TITLE: Preparation of epothilone analogs possessing microtubule stabilizing effects and cytotoxicity
INVENTOR(S): Nicolaou. Kyriacos C.; King. N. Paul; Finlay. M. Ray; He. Yun; Roschangar. Frank; Vourloumis. Dionisios; Vallberg. Hans; Sarabia. Francisco; Ninkovic. Sacha; Hepworth. David; Li. Tianhu
PATENT ASSIGNEE(S): The Scripps Research Institute. USA
SOURCE: U.S.. 59 pp.. Cont.-in-part of U.S. Ser. No. 923.869.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6380394	B1	20020430	US 1998-102602	19980622
US 6441186	B1	20020827	US 1997-923869	19970904
CA 2334342	AA	19991229	CA 1999-2334342	19990621 <--
WO 9967252	A2	19991229	WO 1999-EP4287	19990621 <--
WO 9967252	A3	20000316		
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AU 757854	B2	20030306		
AU 9947752	A1	20000110	AU 1999-47752	19990621 <--
BR 9911420	A	20010320	BR 1999-11420	19990621 <--

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

EP 1089998	A2	20010411	EP 1999-931120	19990621 <--
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RU 2227142	C2	20040420	RU 2000-132188	19990621
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NO 2000006378	A	20010221	NO 2000-6378	20001214 <--
US 2003203938	A1	20031030	US 2003-386999	20030311

PRIORITY APPLN. INFO.:
US 1996-32864P P 19961213
US 1997-856533 B1 19970514
US 1997-923869 A2 19970904
US 1998-102602 A 19980622
US 1999-123155P P 19990306
US 1999-124653P P 19990316
WO 1999-EP4287 W 19990621
WO 1999-EP4299 W 19990621
US 2001-720070 A3 20010419

OTHER SOURCE(S): MARPAT 136:340536
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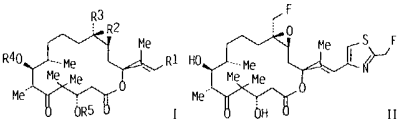


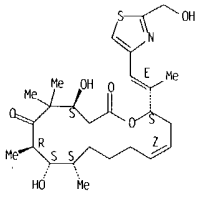
I II

ABSTRACT:
Epothilone analogs. such as I [R1 = heterocycle: R2 = bond. O: R3 = H. Me. CHO. CO2H. ester. amide. CH:CH2. etc.; R4. R5 = H. Me. TBS. TMS]. were prepared and tested for microtubule stabilizing effects and cytotoxicity. Thus. epothilone analog II was prepared via a multistep synthetic sequence starting from trans-3-iodo-2-methylpropenal. 4-bromo-1-butene. (5S)-5.7-bis[[(1.1-dimethylethyl)dimethylsilyl]oxy]-4.4-dimethyl-3-heptanone and 2.4-dibromo-1.3-thiazole. II showed 92% induction of tubulin polymerization and exhibited cytotoxicity IC50 = 2.8 nM and 1.5 nM against taxol-resistant tumor cells PTX 10 and PTX22. resp.

IT **204513-12-2P 204513-35-9P 204513-36-0P**
204513-37-1P 204513-39-3P 204513-40-6P
204513-41-7P 204513-42-8P 204513-43-9P
204513-44-0P 209260-90-2P 209260-91-3P
240816-04-0P 240816-05-1P 240816-06-2P
240816-07-3P 240816-08-4P 240816-09-5P
240816-10-8P 240816-11-9P 240816-12-0P

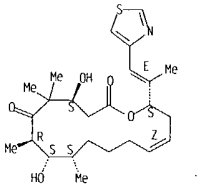
L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
240816-36-8P 240816-37-9P
RL: PAC (Pharmacological activity): RCT (Reactant): SPN (Synthetic preparation): THU (Therapeutic use): BIOL (Biological study): PREP (Preparation): RACT (Reactant or reagent): USES (Uses)
(prepn. of epothilone analogs possessing microtubule stabilizing effects and cytotoxicity)
RN 204513-12-2 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5.5.7.9-tetramethyl-. (4S.7R.8S.9S.13Z.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 204513-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13Z.16S)- (9CI) (CA INDEX NAME)

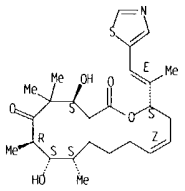
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-36-0 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-

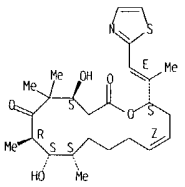
L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-37-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

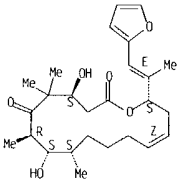
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-39-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(1-piperidinyl)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

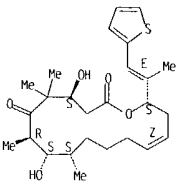
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-42-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

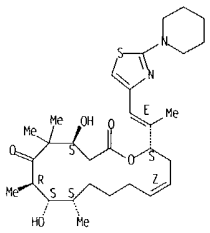
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-43-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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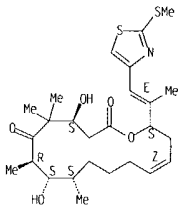
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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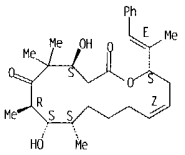
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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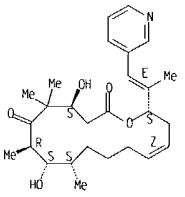
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-90-2 CAPLUS
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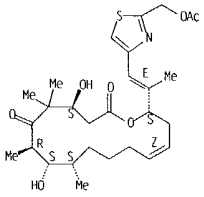
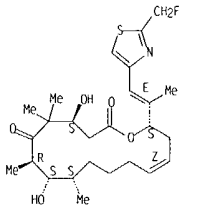
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 209260-91-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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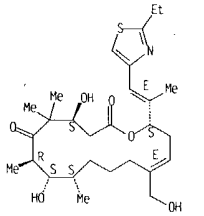
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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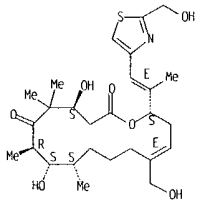
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



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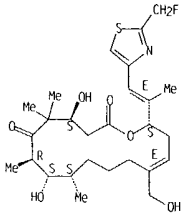
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-05-1 CAPLUS
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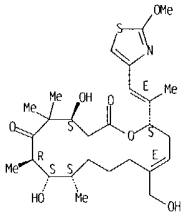
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



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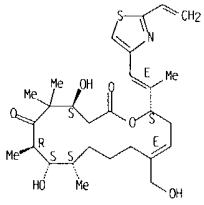
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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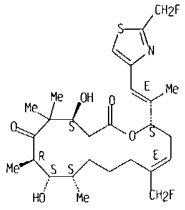
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(fluoromethyl)-16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

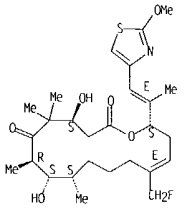
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(fluoromethyl)-4,8-dihydroxy-16-[(1E)-2-(2-methoxy-4-thiazolyl)-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

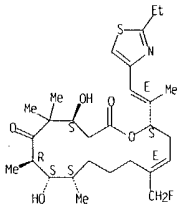
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-11-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethyl-4-thiazolyl)-1-methylethenyl]-13-(fluoromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

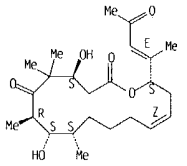
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-12-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethenyl-4-thiazolyl)-1-methylethenyl]-13-(fluoromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

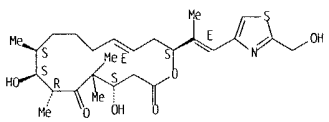
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **204513-14-4P 204513-38-2P 204513-45-1P**
204513-46-2P 204513-47-3P 204513-48-4P
204513-49-5P 204513-50-8P 204513-51-9P
204513-52-0P 204513-53-1P 204513-54-2P
209260-96-8P 209260-97-9P 240816-38-0P
240816-39-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilone analogs possessing microtubule stabilizing effects and cytotoxicity)
RN 204513-14-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

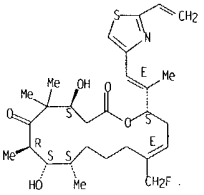
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-38-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[5-(acetyloxy)pentyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

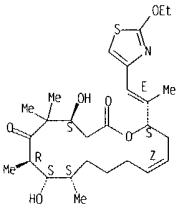
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-36-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethoxy-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

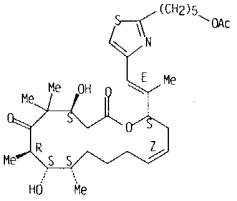
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-37-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-3-oxo-1-butenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

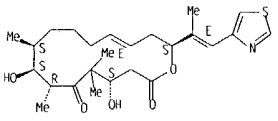
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



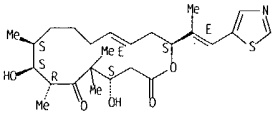
RN 204513-45-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-46-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

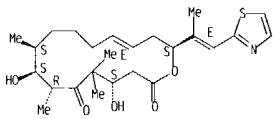
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-47-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-

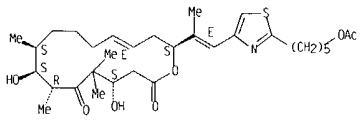
L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-48-4 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 16-[(1E)-2-[2-[5-(acetyloxy)pentyl]-4-thiazolyl]-1-methylethenyl]-4.8-dihydroxy-5.5.7.9-tetramethyl-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

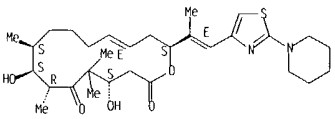
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-49-5 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-[2-(1-piperidinyl)-4-thiazolyl]ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

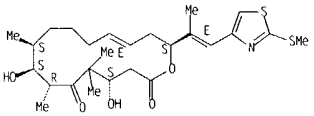
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



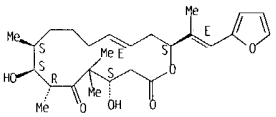
RN 204513-50-8 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-51-9 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4.8-dihydroxy-5.5.7.9-tetramethyl-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

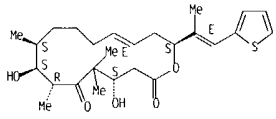
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-52-0 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA

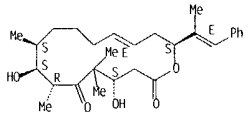
L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



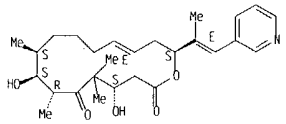
RN 204513-53-1 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-54-2 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

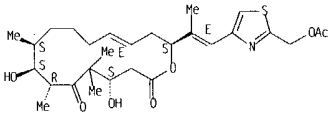
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-96-8 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 16-[(1E)-2-[2-[(acetyloxy)methyl]-4-thiazolyl]-1-methylethenyl]-4.8-dihydroxy-5.5.7.9-tetramethyl-.

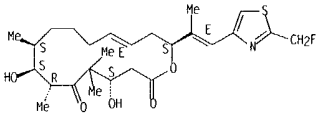
L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



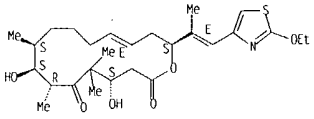
RN 209260-97-9 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4.8-dihydroxy-5.5.7.9-tetramethyl-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 240816-38-0 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 16-[(1E)-2-(2-ethoxy-4-thiazolyl)-1-methylethenyl]-4.8-dihydroxy-5.5.7.9-tetramethyl-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

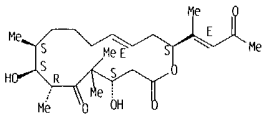
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-39-1 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-3-oxo-1-butenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX

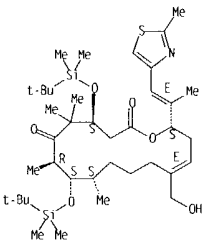
L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **209260-82-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of epothilone analogs possessing microtubule stabilizing effects and cytotoxicity)
RN 209260-82-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

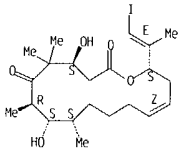
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **204513-16-6P 204513-26-8P 204513-28-0P**
204513-30-4P 240815-87-6P 240816-03-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

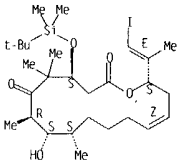
L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(Reactant or reagent)
(prepn. of epothilone analogs possessing microtubule stabilizing effects and cytotoxicity)
RN 204513-16-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



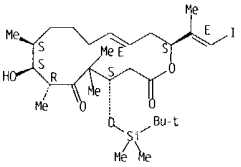
RN 204513-26-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



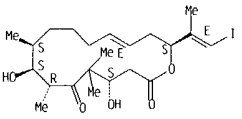
RN 204513-28-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.
Double bond geometry as shown.



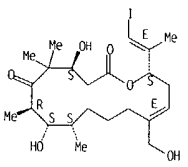
RN 204513-30-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 240815-87-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

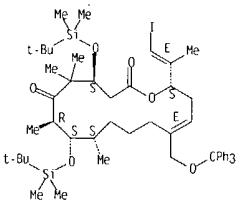
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 5 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 240816-03-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-13-[(triphenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

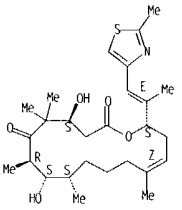


REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:132142 CAPLUS
DOCUMENT NUMBER: 136:309773
TITLE: Synthesis and biological activity of epothilones
AUTHOR(S): Klar, Ulrich; Skuballa, Werner; Buchmann, Bernd; Schwede, Wolfgang; Bunte, Thomas; Hoffmann, Jens; Lichtner, Rosemarie B.
CORPORATE SOURCE: Research Laboratories of Schering AG, Berlin, D-13342, Germany
SOURCE: ACS Symposium Series (2001), 796(Anticancer Agents), 131-147
CODEN: ACSMC8; ISSN: 0097-6156
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review. The total synthesis and biol. activity of epothilone analogs are described. Selected SAR data indicate the possibility to improve activity and selectivity by structural modifications. The new compds. may help to elucidate the therapeutic potential of this class of anticancer drugs.

IT **189453-10-9D**, Epothilone D, analogs
RL: MSC (Miscellaneous)
(review of the synthesis and biol. activity of epothilones)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS

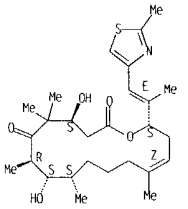
L5 ANSWER 6 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:132141 CAPLUS
DOCUMENT NUMBER: 136:318824
TITLE: Synthetic and semisynthetic analogs of epothilones: chemistry and biological activity
AUTHOR(S): Altmann, Karl-Heinz; Blommers, Marcel J. J.; Caravatti, Giorgio; Florsheimer, Andreas; Nicolaou, Kyriacos C.; O'Reilly, Terrence; Schmidt, Alfred; Schinzer, Dieter; Wartmann, Markus
CORPORATE SOURCE: TA Oncology Research, Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: ACS Symposium Series (2001), 796(Anticancer Agents), 112-130
CODEN: ACSMC8; ISSN: 0097-6156
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Epothilones A and B are naturally occurring microtubule depolymn. inhibitors, which exhibit potent in vitro antiproliferative activity. Epothilone B is a 3-30-fold more potent inhibitor of human cancer cell growth than paclitaxel in paclitaxel-sensitive cancer cell lines and in paclitaxel-resistant lines exceeds paclitaxel activity by 102 - 103-fold. In addition, epothilone B exhibits potent in vivo antitumor activity even in multidrug-resistant tumor models. In order to gain a better understanding of the structural requirements for epothilone-mediated cytotoxicity and antitumor activity and to discover analogs with similar potency but perhaps better tolerability in vivo, we have investigated a series of structural modifications involving the epoxide site (C12/C13) and the heterocyclic side-chain of epothilones. In this paper we present the synthesis of these analogs and we discuss the impact of such modifications on tubulin polymerization activity as well as cytotoxicity in vitro.

IT **189453-10-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthetic and semisynthetic analogs of epothilones and their chemical and biol. activity)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

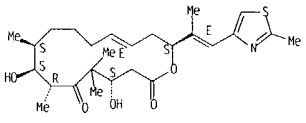
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 7 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **188260-10-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthetic and semisynthetic analogs of epothilones and their chemical and biol. activity)
RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



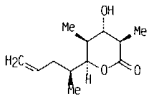
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:123244 CAPLUS
DOCUMENT NUMBER: 136:183657
TITLE: Process for the biomediated preparation of intermediates for use in the synthesis of polyketides, such as epothilone D and discodermolide
INVENTOR(S): Santi, Daniel V.; Ashley, Gary; Myles, David C.
PATENT ASSIGNEE(S): Kosan Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012534	A2	20020214	WO 2001-US25112	20010809
WO 2002012534	A3	20020906		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2001092991	A2	20011206	WO 2001-US17352	20010529 <--
WO 2001092991	A3	20020808		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001083275	A5	20020218	AU 2001-83275	20010809
EP 1307579	A2	20030507	EP 2001-962062	20010809
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:
US 2000-224038P P 20000809
US 2000-237382P P 20001004
US 2000-248387P P 20001113
US 2001-867845 A 20010529

L5 ANSWER 8 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
US 2000-207331P P 20000530
WO 2001-US25112 W 20010809
OTHER SOURCE(S): CASREACT 136:183657; MARPAT 136:183657
GRAPHIC IMAGE:



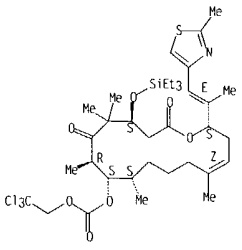
I

ABSTRACT:
The present invention relates to compds., such as I, made by a subset of modules from one or more polyketide synthase ("PKS") genes that are used as starting material in the chemical synthesis of novel mols., particularly naturally occurring polyketides or derivs. thereof. The biol. derived intermediates ("bio-intermediates") generally represent particularly difficult compds. to synthesize using traditional chemical approaches due to one or more stereocenters. In one aspect of the invention, an intermediate in the synthesis of epothilone is provided that feeds into the synthetic protocol of Danishefsky and co-workers. In another aspect of the invention, intermediates in the synthesis of discodermolide are provided that feed into the synthetic protocol of Smith and co-workers. By taking advantage of the inherent stereochem. specificity of biol. processes, the syntheses of key intermediates and thus the overall syntheses of compds. like epothilone and discodermolide are greatly simplified.

IT **241129-40-8P 241129-41-9P**
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(process for the biomediated preparation of intermediates for use in the synthesis of polyketides, such as epothilone D and discodermolide)
RN 241129-40-8 CAPLUS
CN Carbonic acid, (4S,7R,8S,9S,13Z,16S)-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-2,6-dioxo-4-[(triethylsilyl)oxy]oxacyclohexadec-13-en-8-yl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

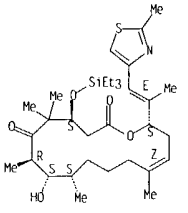
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 8 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 241129-41-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

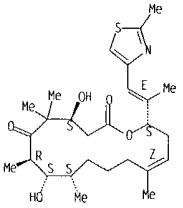
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT 189453-10-9P, Epothilone D
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(process for the biomediated preparation of intermediates for use in the synthesis of polyketides, such as epothilone D and discodermolide)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

L5 ANSWER 8 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



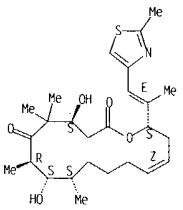
L5 ANSWER 9 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:11427 CAPLUS
DOCUMENT NUMBER: 136:279243
TITLE: Alkyne metathesis: development of a novel molybdenum-based catalyst system and its application to the total synthesis of epothilone A and C
AUTHOR(S): Furstner, Alois; Mathes, Christian; Lehmann, Christian W.
CORPORATE SOURCE: Max-Planck-Institut fur Kohlenforschung, Mulheim/Ruhr, 45470, Germany
SOURCE: Chemistry--A European Journal (2001), 7(24), 5299-5317
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:279243
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
Sterically hindered molybdenum(III) amido complexes of the general type [Mo{(tBu)(Ar)N}3], e.g. I, upon treatment with CH2Cl2 or other halogen donors, have been converted into highly effective catalysts for all kinds of alkyne metathesis reactions. Although the actual nature of the propagating species formed in situ is still elusive, halogen transfer to the Mo center of I plays a decisive role in the activation of such precatalysts. It was possible to isolate and characterize by X-ray crystallog. some of the resulting molybdenum halide derivs., such as II (R = OMe, X = Cl), II (R = Me, X = Cl) and III which themselves were shown to be catalytically active. Numerous applications illustrate the performance of the catalytic system I/CH2Cl2 which operates under mild conditions and tolerates an array of polar functional groups. The wide scope allows the method to be implemented into the total synthesis of sensitive and polyfunctional natural products. Most notable among them is a concise entry into the potent anticancer agents epothilone A and C. The macrolide core of these targets is forged by ring closing alkyne metathesis (RCAM) of diyne IV, followed by Lindlar hydrogenation of the resultant cycloalkyne thus formed. Since this strategy opens a stereoselective entry into (Z)-alkene V, the approach is inherently more efficient than previous syntheses based on conventional RCM.

IT **186692-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

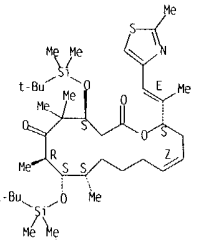
L5 ANSWER 9 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 169 THERE ARE 169 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(alkyne metathesis. development of a novel molybdenum-based catalyst system and its application to the total synthesis of epothilone A and C)
RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **186692-73-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(alkyne metathesis. development of a novel molybdenum-based catalyst system and its application to the total synthesis of epothilone A and C)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

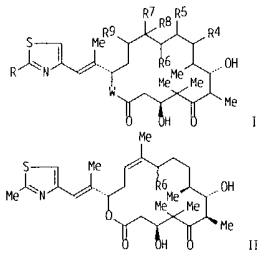
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:886112 CAPLUS
DOCUMENT NUMBER: 136:5855
TITLE: Preparation of epothilone derivatives for pharmaceutical use in the treatment of cancer and other disorders characterized by cellular hyperproliferation
INVENTOR(S): Santi, Daniel; Fardis, Maria; Ashley, Gary
PATENT ASSIGNEE(S): Kosan Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092255	A2	20011206	WO 2001-US15763	20010515 <--
WO 2001092255	A3	20020228		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002045609	A1	20020418	US 2001-859085	20010515

PRIORITY APPLN. INFO.: US 2000-207655P P 20000526
US 2000-218260P P 20000714
US 2000-231552P P 20000911
OTHER SOURCE(S): MARPAT 136:5855
GRAPHIC IMAGE:

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

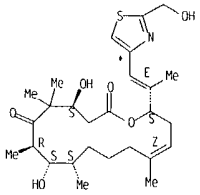
II

ABSTRACT:
Epothilone derivs., such as I [R = Me, CH2OH, CHO; R4 = H, OH, oxo, amino, etc.; R5 = H, OH, oxo; R6 = H, OH, oxo, alkyl, alkylester, halogen, etc.; R7 = H, alkyl, halogen, hydroxyalkyl, alkoxyalkyl, arylalkyl, heterocyclylalkyl, etc.; R8 = R9 = H; R8R9 = bond; O; R5R6 = bond; W = O; NR11; R11 = H, alkyl, aryl], were prepared for therapeutic use in the treatment of cancer and non-cancer disorders characterized by cellular hyperproliferation. Thus, (11S)-hydroxyepothilone D II (R6 = α-OH) and its (11R)-diastereomer II (R = β-OH) were prepared by hydroxylation of epothilone D using SeO2 and Me3COOH by stirring in CH2Cl2 for 48 h. The prepared epothilone derivs. were assayed for cyctotoxicity against MCF-7 breast, MDR breast, SF-268 glioma and NCI-H460 lung cancer cell lines and were assayed for tubulin polymerization inhibition.

IT **252981-50-3P**
RL: BPN (Biosynthetic preparation); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and formulation of epothilone derivs. for pharmaceutical use in the treatment of cancer and other disorders characterized by cellular hyperproliferation)
RN 252981-50-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

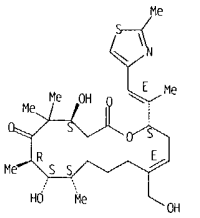
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



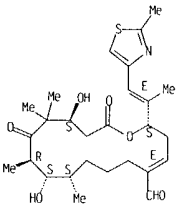
IT **201136-64-3P 201136-85-8P 240816-07-3P**
377085-63-7P 377085-66-0P 377085-79-5P
RL: OMA (Drug mechanism of action); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and formulation of epothilone derivs. for pharmaceutical use in the treatment of cancer and other disorders characterized by cellular hyperproliferation)
RN 201136-64-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



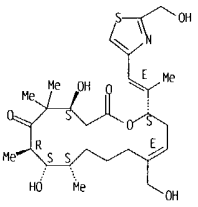
L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 201136-85-8 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxaldehyde, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-07-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

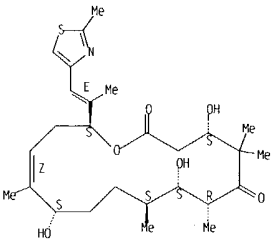
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 377085-63-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8,12-trihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,12S,13Z,16S)- (9CI) (CA INDEX NAME)

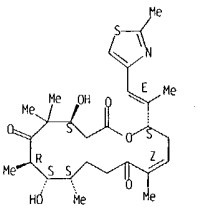
Absolute stereochemistry.

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 377085-66-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6,12-trione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

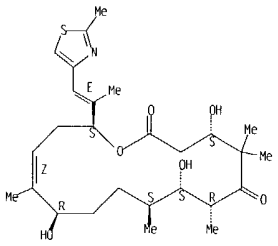
Absolute stereochemistry.
Double bond geometry as shown.



RN 377085-79-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8,12-trihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,12R,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



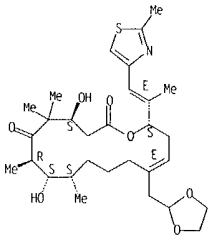
IT **198475-07-9P 240816-09-5P 371979-73-6DP,**
conjugate with poly(L-glutamic acid) **377085-73-9P**
377085-74-0P 377085-75-1P 377085-78-4DP,
conjugate with an anti-tubulin antibody
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and formulation of epothilone derivs. for pharmaceutical use in the treatment of cancer and other disorders characterized by cellular hyperproliferation)

RN 198475-07-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 13-(1,3-dioxolan-2-ylmethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

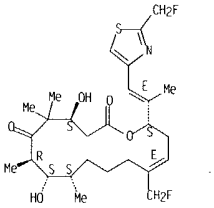
L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-09-5 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 13-(fluoromethyl)-16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

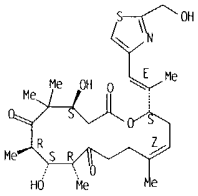


RN 371979-73-6 CAPLUS

CN Oxacyclohexadec-13-ene-2,6,10-trione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9R,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

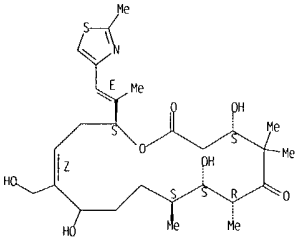
L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 377085-73-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8,12-trihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

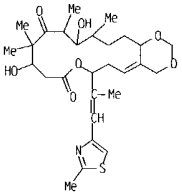
Absolute stereochemistry.
Double bond geometry as shown.



RN 377085-74-0 CAPLUS

CN 4H,9H-1,3-Dioxino[5,4-e]oxacyclohexadecin-9,13(10H)-dione, 6,7,11,12,14,15,16,17,18,18a-decahydro-11,15-dihydroxy-12,12,14,16-tetramethyl-7-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4aZ,7S,11S,14R,15S,16S)- (9CI) (CA INDEX NAME)

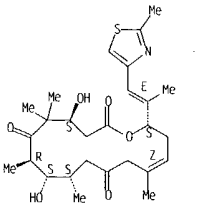
L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 377085-75-1 CAPLUS

CN Oxacyclohexadec-13-ene-2,6,11-trione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

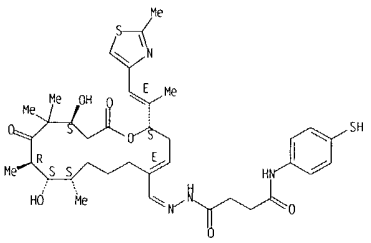


RN 377085-78-4 CAPLUS

CN Butanoic acid, 4-[(4-mercaptophenyl)amino]-4-oxo-, [[(2S,4E,9S,10S,11R,14S)-10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxooxacyclohexadec-4-en-5-yl]methylene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

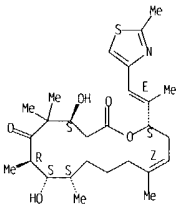


IT **189453-10-9 371979-42-9 371979-73-6**
377085-95-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and formulation of epothilone derivs. for pharmaceutical use in the treatment of cancer and other disorders characterized by cellular hyperproliferation)

RN 189453-10-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

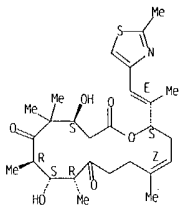


RN 371979-42-9 CAPLUS

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CN Oxacyclohexadec-13-ene-2,6,10-trione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13Z,16S)-(9CI) (CA INDEX NAME)

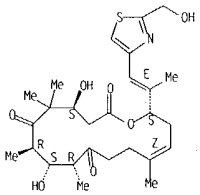
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 371979-73-6 CAPLUS

CN Oxacyclohexadec-13-ene-2,6,10-trione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9R,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

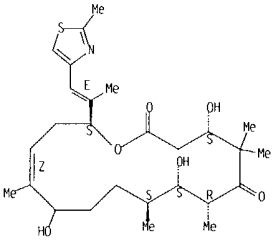


RN 377085-95-5 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8,12-trihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.
Double bond geometry as shown.



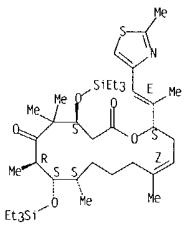
IT **247230-54-2P 377085-67-1P 377085-81-9P**
377085-82-0P 377085-83-1P 377085-84-2P
377085-85-3P 377085-86-4P 377085-88-6P
377085-89-7P 377085-91-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and formulation of epothilone derivs. for pharmaceutical use in the treatment of cancer and other disorders characterized by cellular hyperproliferation)

RN 247230-54-2 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

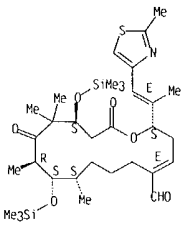
L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 377085-67-1 CAPLUS

CN Oxacyclohexadec-4-ene-5-carboxaldehyde, 9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-10,14-bis[(trimethylsilyl)oxy]-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

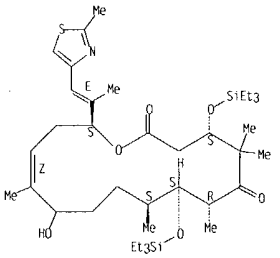


RN 377085-81-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 12-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

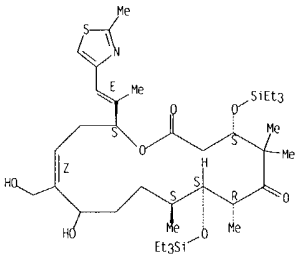
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 377085-82-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 12-hydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

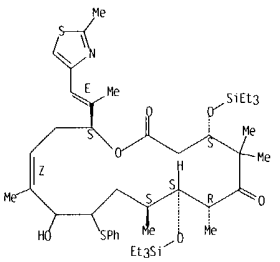
Absolute stereochemistry.
Double bond geometry as shown.



RN 377085-83-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6,12-trione, 5,5,7,9,13-pentamethyl-16-[(1E)-1-

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 12-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-11-(phenylthio)-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

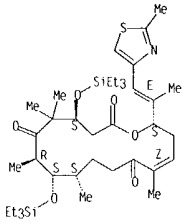


RN 377085-86-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12-[(methylsulfonyl)oxy]-11-(phenylthio)-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

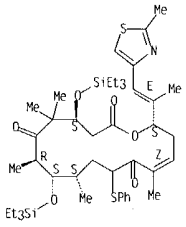
L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



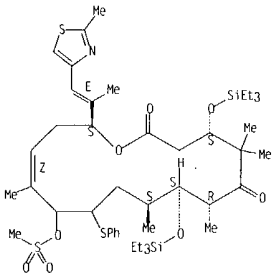
RN 377085-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6,12-trione, 5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-11-(phenylthio)-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



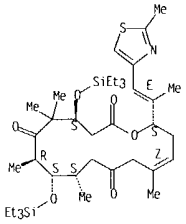
RN 377085-85-3 CAPLUS

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 377085-88-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6,11-trione, 5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

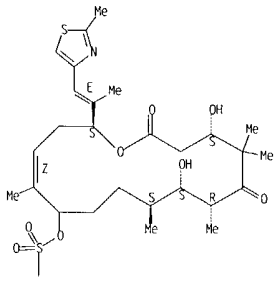


RN 377085-89-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12-[[(4-methylphenyl)sulfonyl]oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

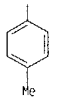
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

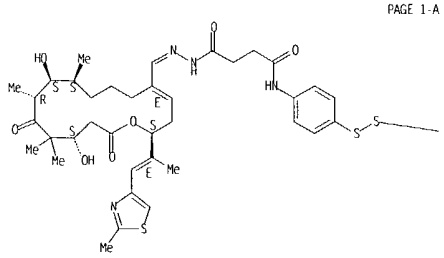


RN 377085-91-1 CAPLUS
CN Butanoic acid, 4-oxo-4-[[4-(2-pyridinyldithio)phenyl]amino]-, [[(2S,4E,9S,10S,11R,14S)-10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxooxacyclohexadec-4-en-5-yl]methylene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

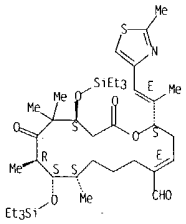


PAGE 1-B

IT 377085-65-9P 377085-68-2P 377085-80-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and formulation of epothilone derivs. for pharmaceutical use in the treatment of cancer and other disorders characterized by cellular hyperproliferation)
RN 377085-65-9 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxaldehyde, 9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-10,14-bis[(triethylsilyl)oxy]-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

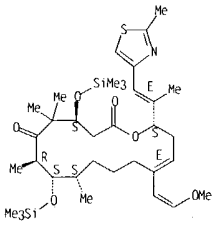
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 377085-68-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(2-methoxyethenyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(trimethylsilyl)oxy]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

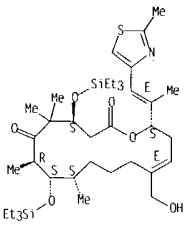
Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 377085-80-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 10 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

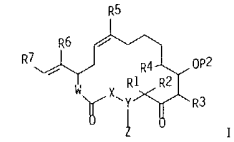


L5 ANSWER 11 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:843887 CAPLUS
DOCUMENT NUMBER: 135:371566
TITLE: Process for reduction of oxiranyl epothilones to olefinic epothilones
INVENTOR(S): Kim, Soong-hoon; Johnson, James A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 170,581.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

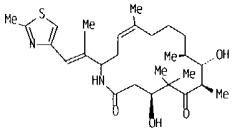
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6320045	B1	20011120	US 1999-316796	19990521 <--
WO 2000071521	A1	20001130	WO 2000-US13253	20000515 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1178968	A1	20020213	EP 2000-930725	20000515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500394	T2	20030107	JP 2000-619778	20000515

PRIORITY APPLN. INFO.: US 1997-67549P P 19971204
US 1998-82563P P 19980421
US 1998-170581 A2 19981013
US 1999-316796 A 19990521
WO 2000-US13253 W 20000515
OTHER SOURCE(S): CASREACT 135:371566; MARPAT 135:371566
GRAPHIC IMAGE:

L5 ANSWER 11 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I



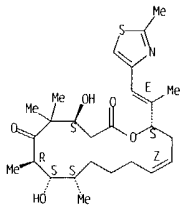
II

ABSTRACT:
This process produced epothilones I (W = O, NR8; R1-R6 = H, (un)substituted alkyl or aryl and R1 and R2 can be cycloalkyl; R7 = H, (un)substituted alkyl, aryl, cycloalkyl or 4-7 membered heterocyclic N-, O-, or S-containing rings; R8 = H, (un)unsubstituted alkyl, OH, (un)unsubstituted O-alkyl; X = CH2 or XY = CH=CH; Z = H or OP1 where P1, P2 = H, (un)substituted alkyl, alkanoyl, aroyl, trialkyl(aryl)silyl) from oxiranyl epothilones via the reaction of the oxiranyl moiety with a metal or metal-assisted reagent selected from the group consisting of reactive metallocenes, or (WCl6, n-BuLi). Thus II was prepared in 29% yield in a multistep reaction from epothilone B via the aminoheptadecenoic acid that cyclized to the oxiranyl azaepothilone intermediate which was reacted with WCl6 in THF and n-BuLi in hexane.

IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
226956-19-0P, Bis(triethylsilyl)epothilone C
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for reduction of oxiranyl epothilones to olefinic epothilones)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

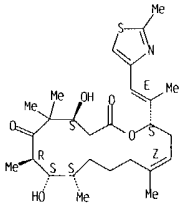
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 11 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

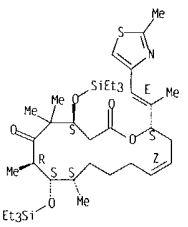
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 226956-19-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 11 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:816957 CAPLUS
DOCUMENT NUMBER: 135:343416
TITLE: Production of polyketides
INVENTOR(S): Arslanian, Robert L.; Ashley, Gary; Frykman, Scott; Julien, Bryan; Katz, Leonard; Khosla, Chaitan; Lau, Janice; Licardi, Peter J.; Regentin, Rika; Santi, Daniel; Tang, Li
PATENT ASSIGNEE(S): Kosan Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083800	A2	20011108	WO 2001-US13793	20010426 <--
WO 2001083800	C1	20030103		
WO 2001083800	A3	20030410		
WO 2001083800	C2	20030912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6410301	B1	20020625	US 2000-560367	20000428
US 2002156110	A1	20021024	US 2001-825876	20010403
US 6589968	B2	20030708		
US 6489314	B1	20021203	US 2001-825856	20010403
US 2002193361	A1	20021219		
AU 2001095195	A5	20011112	AU 2001-95195	20010426 <--
EP 1320611	A2	20030625	EP 2001-973782	20010426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004508810	T2	20040325	JP 2001-580407	20010426
US 2003073205	A1	20030417	US 2001-957483	20010919

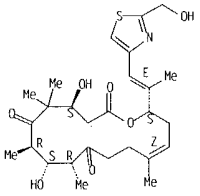
PRIORITY APPLN. INFO.: US 2000-560367 A 20000428
US 2000-232696P P 20000914
US 2000-257517P P 20001221
US 2001-269020P P 20010213
US 2001-825856 A 20010403
US 2001-825876 A 20010403

L5 ANSWER 12 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
US 1998-109401P P 19981120
US 1999-119386P P 19990210
US 1999-122620P P 19990303
US 1999-130560P P 19990422
US 1999-443501 A2 19991119
WO 1999-US27438 A2 19991119
WO 2001-US13793 W 20010426

OTHER SOURCE(S): MARPAT 135:343416
ABSTRACT:
Recombinant Myxococcus host cells can be used to produce polyketides, including epothilone and epothilone analogs that can be purified from the fermentation broth and crystallized

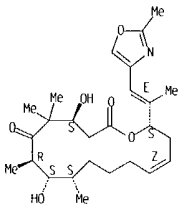
IT 371979-73-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of poly(1-glutamic acid)-21-hydroxy-9-oxoepothilone D conjugate)
RN 371979-73-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6,10-trione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9R,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



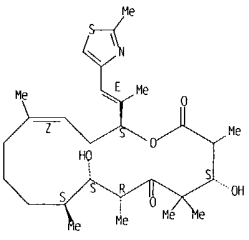
IT 198475-12-6P 371979-55-4P 371979-56-5P
371979-59-8P 371979-60-1P 371979-61-2P
371979-62-3P 371979-63-4P 371979-64-5P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(production of polyketides using recombinant Myxococcus host cells)
RN 198475-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 371979-55-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-3,5,5,7,9,13-hexamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

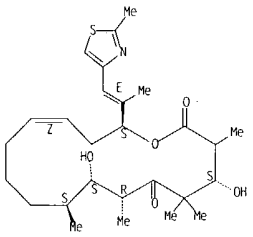
Absolute stereochemistry.
Double bond geometry as shown.



RN 371979-56-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-3,5,5,7,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

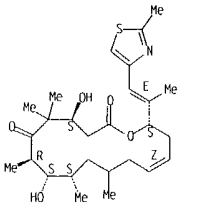
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 12 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 371979-59-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,11-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

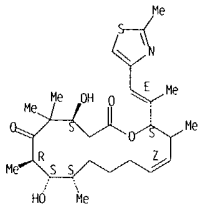
Absolute stereochemistry.
Double bond geometry as shown.



RN 371979-60-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,15-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

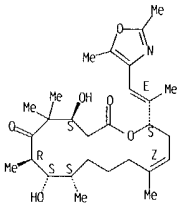
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 12 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 371979-61-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2,5-dimethyl-4-oxazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

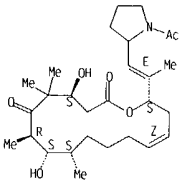
Absolute stereochemistry.
Double bond geometry as shown.



RN 371979-62-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2,5-dimethyl-4-oxazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

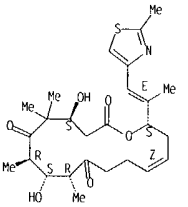
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 12 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



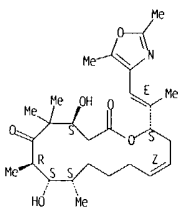
IT 371979-54-3P
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(production of polyketides using recombinant Myxococcus host cells)
RN 371979-54-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6,10-trione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



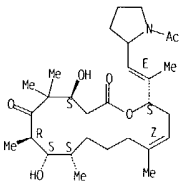
IT 198571-09-4P 371979-42-9P 371979-44-1P
371979-45-2P 371979-49-6P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(production of therapeutic polyketides using recombinant Myxococcus host cells)
RN 198571-09-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 12 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 371979-63-4 CAPLUS
CN Pyrrolidine, 1-acetyl-2-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-10,14-dihydroxy-5,9,11,13,13-pentamethyl-12,16-dioxooxacyclohexadec-4-en-2-yl]-1-propenyl]- (9CI) (CA INDEX NAME)

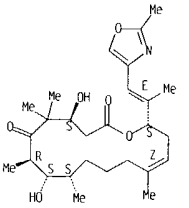
Absolute stereochemistry.
Double bond geometry as shown.



RN 371979-64-5 CAPLUS
CN Pyrrolidine, 1-acetyl-2-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-10,14-dihydroxy-9,11,13,13-tetramethyl-12,16-dioxooxacyclohexadec-4-en-2-yl]-1-propenyl]- (9CI) (CA INDEX NAME)

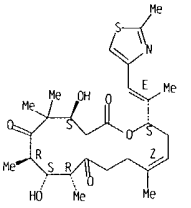
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 12 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 371979-42-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6,10-trione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13Z,16S)- (9CI) (CA INDEX NAME)

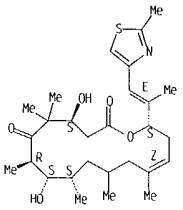
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 371979-44-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,11,13-hexamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

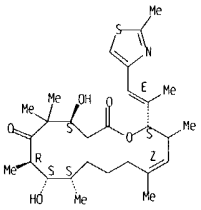
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 12 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 371979-45-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13,15-hexamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

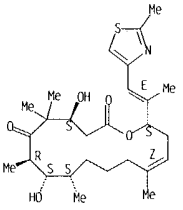


RN 371979-49-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13,15-hexamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

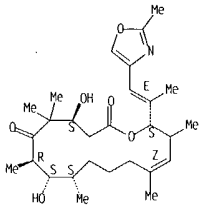
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 12 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

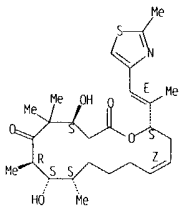


L5 ANSWER 12 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(production of therapeutic polyketides using recombinant Myxococcus host cells)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

L5 ANSWER 13 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:791275 CAPLUS
DOCUMENT NUMBER: 136:167194
TITLE: Total syntheses of epothilones B and D: applications of allylstannanes in organic synthesis
AUTHOR(S): Martin, Nathaniel; Thomas, Eric J.
CORPORATE SOURCE: The Department of Chemistry, The University of Manchester, Manchester, M13 9PL, UK
SOURCE: Tetrahedron Letters (**2001**), 42(47), 8373-8377
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:167194
GRAPHIC IMAGE:

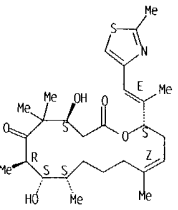
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
Following exploratory studies which culminated in syntheses of the alc. I (corresponding to the C(7)-C(15) fragment of epothilone D), a total synthesis of epothilones B and D is reported in which the trisubstituted 12,13-double-bond is introduced stereoselectively using the tin(IV) bromide-promoted reaction between the allylstannane and the PMB-protected (3R)-4-hydroxy-3-methylbutanal. A Barton deoxygenation then gave the C(7)-C(15) fragment. After development of the thiazole-aldehyde containing side-chain, an aldol condensation with the Et ketone II gave the adduct III which was taken through to epothilone D and then to epothilone B.

IT **189453-10-9P**, Epothilone D **189453-35-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilones B and D)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

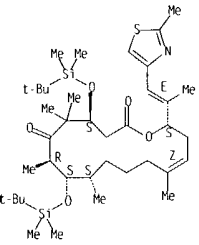
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 13 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

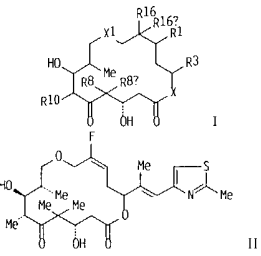
ACCESSION NUMBER: 2001:780370 CAPLUS
DOCUMENT NUMBER: 135:331294
TITLE: Preparation of epothilone derivatives for pharmaceutical use in the treatment of cancer
INVENTOR(S): Buchmann, Bernd; Klar, Ulrich; Skuballa, Werner; Schwede, Wolfgang; Hoffmann, Jens; Lichtner, Rosemarie
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 42 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10020517	A1	20011025	DE 2000-10020517	20000419 <--
WO 2001081342	A2	20011101	WO 2001-EP4552	20010419 <--
WO 2001081342	A3	20020510		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1276740	A2	20030122	EP 2001-936262	20010419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003531207	T2	20031021	JP 2001-578432	20010419
NO 2002005029	A	20021018	NO 2002-5029	20021018
US 2004058969	A1	20040325	US 2002-257925	20021018

PRIORITY APPLN. INFO.: DE 2000-10020517 A 20000419
WO 2001-EP4552 W 20010419

OTHER SOURCE(S): MARPAT 135:331294
GRAPHIC IMAGE:

L5 ANSWER 14 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

II

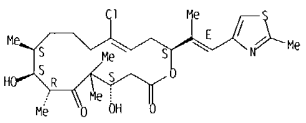
ABSTRACT:
Epothilones, such as I [R3 = heteroaryl, heteroarylalkenyl, heteroarylhaloalkenyl,etc.; R8, R8a = H, alkyl, arylalkyl; R8R8a = alkylene, heteroalkene; R10 = H, alkyl, alkenyl, alkynyl; R1R16a = bond, O; R16 = H, CN, alkyl, halogen; X = O, NH; X1 = O, CH2], were prepared for a variety of therapeutic uses, such as treatment of malignant tumors, proliferative diseases, leukemia, and chronic inflammatory diseases. Thus, epothilone II was prepared via a multistep synthetic sequence starting from (3S)-dihydro-3-hydroxy-4,4-dimethyl-2(3H)-furanone, L-(-)-malic acid, and [(2-methyl-4-thiazolyl)methyl]phosphonic acid di-Et ester. Pharmaceutical formulations of the prepared oxa-epothilones were discussed, but specific biol. activity data was not presented.

IT **369646-16-2P 369646-18-4P 369646-24-2P**
369646-26-4P 369646-31-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilone derivs. for pharmaceutical use in the treatment of cancer)

RN 369646-16-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-chloro-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

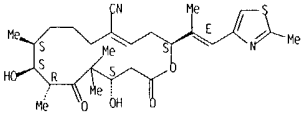
Absolute stereochemistry.
Double bond geometry as described by E or Z.

L5 ANSWER 14 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



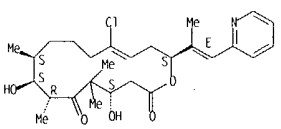
RN 369646-18-4 CAPLUS
CN Oxacyclohexadec-4-ene-5-carbonitrile, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 369646-24-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-chloro-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,16S)-(9CI) (CA INDEX NAME)

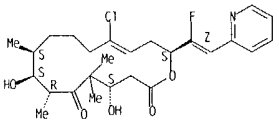
Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 369646-26-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-chloro-16-[(1Z)-1-fluoro-2-(2-pyridinyl)ethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,16S)-(9CI) (CA INDEX NAME)

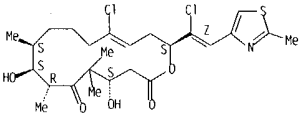
Absolute stereochemistry.
Double bond geometry as described by E or Z.

L5 ANSWER 14 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 369646-31-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-chloro-16-[(1Z)-1-chloro-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



L5 ANSWER 15 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:752384 CAPLUS
DOCUMENT NUMBER: 136:37430
TITLE: Total synthesis of epothilone B
AUTHOR(S): Valluri, Muralikrishna; Hindupur, Rama M.; Bijoy, Panicker; Labadie, Guillermo; Jung, Jae-Chul; Avery, Mitchell A.
CORPORATE SOURCE: Department of Medicinal Chemistry School of Pharmacy Department of Chemistry and National Center for Natural Products Research, University of Mississippi, University, MS, 38677-1848, USA
SOURCE: Organic Letters (2001), 3(23), 3607-3609
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:37430
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

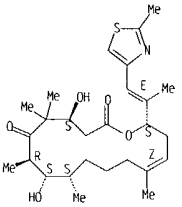
ABSTRACT:
A convergent and stereoselective total synthesis of epothilone B (I) is described. The key steps are Normant reaction, Wadsworth-Emmons reaction of a Me ketone II with the phosphonate reagent III, diastereoselective aldol condensation of aldehyde IV with enolate V to form the C6-C7 bond, and macrolactonization.

IT **189453-10-9P**, Epothilone D **380605-93-6P**
380605-94-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective total synthesis of epothilone B via Normant, Wadsworth-Emmons, diastereoselective aldol, and macrolactonization reactions)

RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

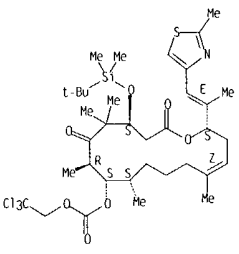
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 15 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 380605-93-6 CAPLUS
CN Carbonic acid, (4S,7R,8S,9S,13Z,16S)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-2,6-dioxooxacyclohexadec-13-en-8-yl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

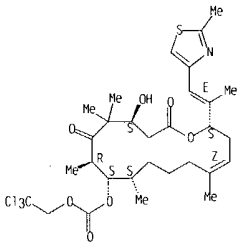
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 380605-94-7 CAPLUS
CN Carbonic acid, (4S,7R,8S,9S,13Z,16S)-4-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-2,6-dioxooxacyclohexadec-13-en-8-yl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 15 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:731069 CAPLUS
DOCUMENT NUMBER: 135:287591
TITLE: Preparation of epothilone intermediates
INVENTOR(S): Vite, Gregory D.; Kim, Soong-Hoon; Hoeefle, Gerhard
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

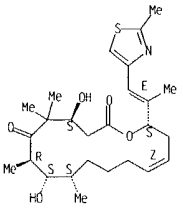
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001073103	A2	20011004	WO 2001-US9620	20010323 <--
WO 2001073103	A3	20020523		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002042109	A1	20020411	US 2001-811808	20010319
US 6593115	B2	20030715		
US 2004023345	A1	20040205	US 2003-447082	20030528

PRIORITY APPLN. INFO.: US 2000-191975P P 20000324
US 2001-811808 A3 20010319
OTHER SOURCE(S): CASREACT 135:287591; MARPAT 135:287591
ABSTRACT:
The present invention relates to a process for the preparation of intermediates useful in the synthesis of epothilone analogs by initially enzymically degrading certain epothilone compds. to form ring-open structures containing a carboxyl group which is esterified, the hydroxyl groups on the moiety protected and the resulting compound oxidized by, e.g. ozone, to form a first intermediate. The first intermediate can be reacted with a triphenylphosphine adduct to yield a compound containing an ester group at position 1 which is subsequently hydrolyzed to form a second intermediate.

IT **186692-73-9**, Epothilone C
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(preparation of epothilone intermediates)
RN 186692-73-9 CAPLUS

L5 ANSWER 16 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

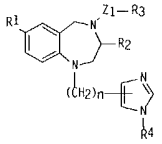
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



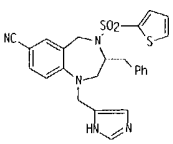
L5 ANSWER 17 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:730715 CAPLUS
DOCUMENT NUMBER: 135:288636
TITLE: Synergistic methods and compositions for treating cancer using two or more anticancer agents
INVENTOR(S): Lee, Francis Y.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072721	A2	20011004	WO 2001-US9193	20010322 <--
WO 2001072721	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1272193	A2	20030108	EP 2001-920653	20010322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003528864	T2	20030930	JP 2001-570634	20010322
US 2002002162	A1	20020103	US 2001-817456	20010326
US 6537988	B2	20030325		
NO 2002004610	A	20021125	NO 2002-4610	20020926

PRIORITY APPLN. INFO.: US 2000-192278P P 20000327
WO 2001-US9193 W 20010322
OTHER SOURCE(S): MARPAT 135:288636
GRAPHIC IMAGE:



I

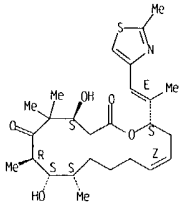


II

L5 ANSWER 17 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
ABSTRACT:
The present invention provides a synergistic method for the treatment of cancer which comprises administering a synergistically, therapeutically effective amount of: (i) at least agent selected from the group consisting of cytotoxic agents and cytostatic agents, and (ii) a compound of formula [I: R1 = Cl, Br, CN, substituted Ph, substituted pyridyl; R2 = alkyl, aralkyl; R3,R5 = substituted alkyl, aryl, heterocycle; R4 = H, alkyl; Z1 = CO, SO2, CO2, SO2N(R5); n = 1,2] or a pharmaceutically acceptable salt thereof. The present invention further provides a pharmaceutical composition for the synergistic treatment of cancer which comprises at least one agent selected from the group consisting of antiproliferative cytotoxic agents and antiproliferative cytostatic agents, a compound of formula I, and a pharmaceutically acceptable carrier. Synergism was observed when non-proliferating tumor cells were treated with diazepine II·HCl and paclitaxel (III) simultaneously or when III preceded II·HCl.

IT **186692-73-9**, Epothilone C **189453-10-9**, Epothilone D
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic methods using two or more anticancer agents for treating cancer)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

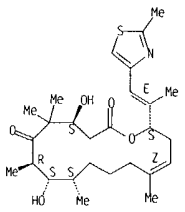
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



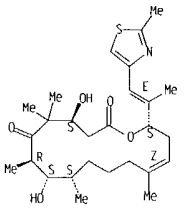
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 17 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



L5 ANSWER 18 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

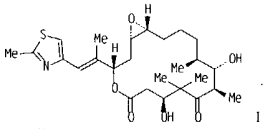


REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

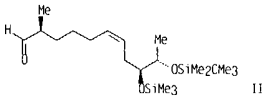
L5 ANSWER 18 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:729040 CAPLUS
DOCUMENT NUMBER: 136:95676
TITLE: Subcellular distribution of epothilones in human tumor cells
AUTHOR(S): Lichtner, R. B.; Rotgeri, A.; Bunte, T.; Buchmann, B.; Hoffmann, J.; Schwede, W.; Skuballa, W.; Klar, U.
CORPORATE SOURCE: Research Laboratories of Schering AG, Berlin, 13342, Germany
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(20), 11743-11748
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Epothilones are a new class of natural and potent antineoplastic agents that stabilize microtubules. Although 12,13-epoxide derivs. are potent antiproliferative agents, the activities of the corresponding 12,13-olefin analogs are significantly decreased. These data were confirmed for two new analogs, 6-propyl-EpoB (pEB) and 6-propyl-EpoD (pED), in comparison with the natural compds. EpoB/EpoD, by using human A431, MCF7, and MDR1-overexpressing NCI/Adr cells. By using tritiated pEB/pED, compound uptake, release, and nuclear accumulation were investigated in A431 and NCI/Adr cells. In these cells, epothilones can principally be recognized and exported by verapamil-sensitive efflux pumps, which are not identical to MDR1. The degree of export depends on the structure, olefin vs. epoxide-analog, and also on the intracellular drug concentration. The accumulation of pED used at 3.5 or 70 nM, resp., was increased in the presence of 10 μM Verapamil in both cell lines 2- to 8-fold. In contrast, the intracellular levels of pEB were affected by Verapamil only at 3.5 nM pEB in NCI/Adr (2-fold) and not in A431 cells. In addition, strong nuclear accumulation was observed for pEB (40-50%) but not paclitaxel or pED (5-15%) in both cell lines. Our study suggests that differences in growth inhibitory efficacy between epoxide and olefin analogs may be based on different mechanisms of drug accumulation and subcellular distribution.

IT **189453-10-9**, Epothilone D
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(subcellular distribution of antitumor epothilones in human tumor cells)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

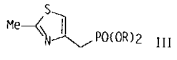
L5 ANSWER 19 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:708494 CAPLUS
DOCUMENT NUMBER: 136:69672
TITLE: Total synthesis of epothilone A
AUTHOR(S): Hindupur, R. M.; Panicker, B.; Valluri, M.; Avery, M. A.
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Mississippi, School of Pharmacy, University, MS, 38677-1848, USA
SOURCE: Tetrahedron Letters (2001), 42(42), 7341-7344
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:69672
GRAPHIC IMAGE:



I



II



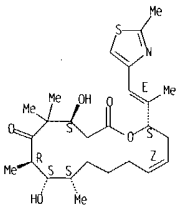
III

ABSTRACT:
A convergent total synthesis of epothilone A (I) is described. The key steps are diastereoselective aldol condensation of aldehyde II to form the C6-C7 bond; macrolactonization and Wadsworth-Emmons reaction of Me ketone with phosphonate reagent III (R = Et).

IT **186692-73-9P 186692-84-2P 383912-04-7P**
383912-05-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of epothilone A via stereoselective aldol.

L5 ANSWER 19 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
macrolactonization, and Wadsworth-Emmons reactions)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

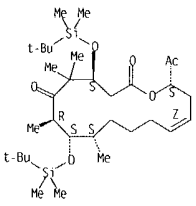
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

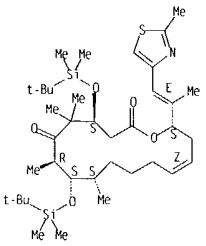
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 19 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



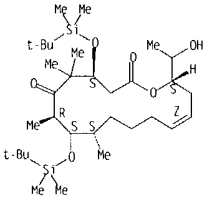
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 383912-04-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-(1-hydroxyethyl)-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 383912-05-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-acetyl-4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

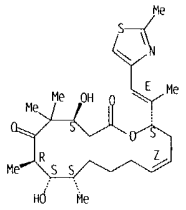
L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:688078 CAPLUS
DOCUMENT NUMBER: 136:34199
TITLE: Synthesis of epothilone analogues by antibody-catalyzed resolution of thiazole aldol synthons on a multigram scale. Biological consequences of C-13 alkylation of epothilones
AUTHOR(S): Sinha, Subhash C.; Sun, Jian; Wartmann, Markus; Lerner, Richard A.
CORPORATE SOURCE: Department of Molecular Biology, The Scripps Research Institute and The Skaggs Institute for Chemical Biology, La Jolla, CA, 92037, USA
SOURCE: ChemBioChem (**2001**), 2(9), 656-665
CODEN: CBCHFX; ISSN: 1439-4227
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Three monoclonal aldolase antibodies (84G3, 85H6, and 93F3), generated against a β-diketone hapten by the reactive immunization technique, catalyzed highly enantioselective retro-aldol reactions of the racemic thiazole aldols. Antibody 84G3 (0.0004-0.005 mol%) was used to resolve racemic thiazole aldols in multigram quantities. Multiple alkyl analogs of epothilone and their trans isomers were synthesized starting from thiazole aldols. Construction of the trisubstituted olefin moieties was catalyzed by Grubbs' catalyst. Initial biol. testing showed appreciable tubulin polymerization and antiproliferative activities that approached those of epothilone C. The most active compound even displayed potencies comparable to those observed for epothilones A and D. Interestingly, all trans analogs were more potent than their corresponding cis isomers. While introduction of an alkyl group in the cis series led to an overall reduction in biol. activity (compared to epothilone C), appropriate modification of the thiazole moiety (replacement of the 2-Me substituent by a 2-methylthio group) was able to compensate for this loss. These results are encouraging in view of the expectation that epoxidns. of these compds. should further increase their cellular activities.

IT **186692-73-9**, Epothilone C **189453-10-9**, Epothilone D
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis of epothilone analogs by antibody-catalyzed resolution of thiazole aldol synthons on a multigram scale)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

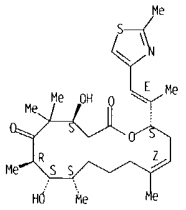
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

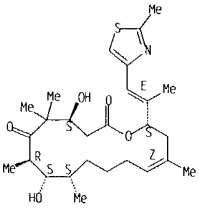
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT 253447-39-1P 253447-56-2P 253447-71-1P
253447-83-5P 334934-75-7P 334934-76-8P
334934-81-5P 334934-82-6P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of epothilone analogs by antibody-catalyzed resolution of thiazole aldol synthons on a multigram scale)
RN 253447-39-1 CAPLUS

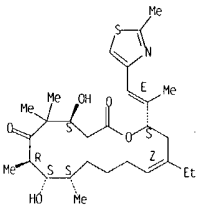
L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 253447-56-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

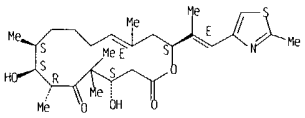
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 253447-71-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-

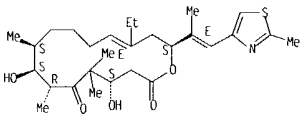
L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 253447-83-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

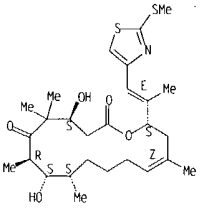
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 334934-75-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

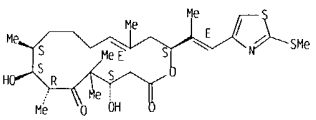
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 334934-76-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

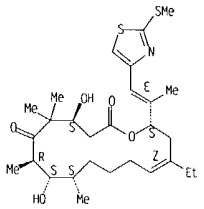
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 334934-81-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

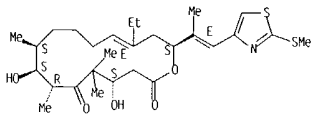
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 334934-82-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.

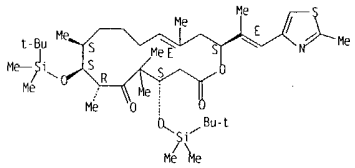


IT **253448-16-7P 253448-18-9P 380430-11-5P**
380430-12-6P 380430-13-7P 380430-14-8P
380430-15-9P 380430-16-0P 380430-17-1P
380430-18-2P 380430-19-3P 380430-20-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilone analogs by antibody-catalyzed resolution of thiazole aldol synthons on a multigram scale)

RN 253448-16-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

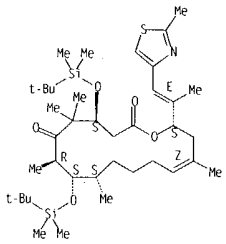
Absolute stereochemistry.

L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as described by E or Z.



RN 253448-18-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

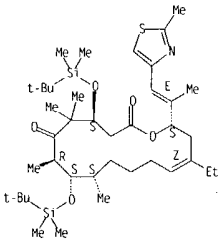
Absolute stereochemistry.
Double bond geometry as shown.



RN 380430-11-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-ethyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

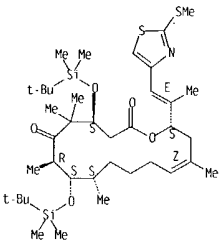
Absolute stereochemistry.

L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



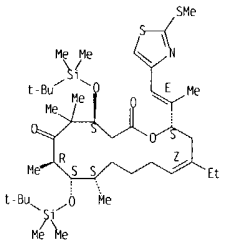
RN 380430-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



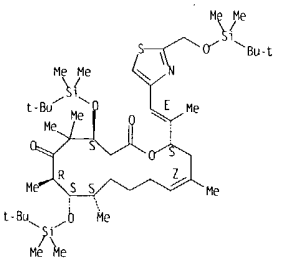
RN 380430-13-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-ethyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.
Double bond geometry as shown.



RN 380430-14-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-[2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-thiazolyl]-1-methylethenyl]-5,5,7,9,14-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

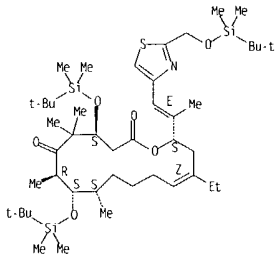
Absolute stereochemistry.
Double bond geometry as shown.



RN 380430-15-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-[2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-thiazolyl]-1-methylethenyl]-14-

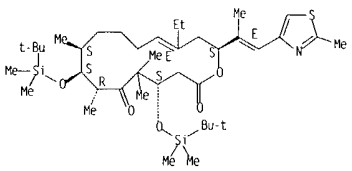
L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
ethyl-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



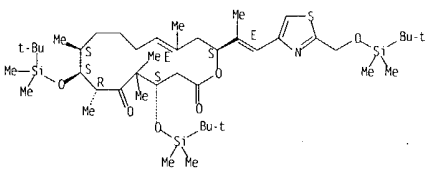
RN 380430-16-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-ethyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



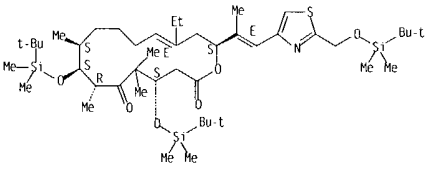
RN 380430-17-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-

L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 380430-20-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-[2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-thiazolyl]-1-methylethenyl]-14-ethyl-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

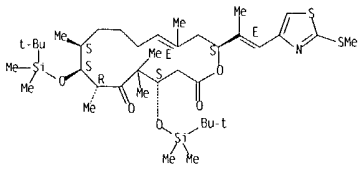


IT 334934-87-1P 334934-88-2P 334934-97-3P
334934-98-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of epothilone analogs by antibody-catalyzed resolution of thiazole aldol synthons on a multigram scale)
RN 334934-87-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

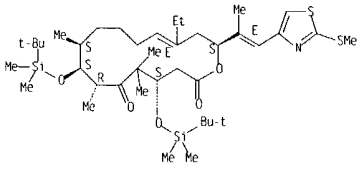
L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 380430-18-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-ethyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

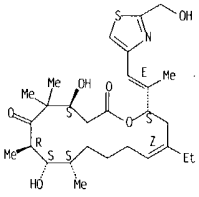
Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 380430-19-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-[2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-thiazolyl]-1-methylethenyl]-5,5,7,9,14-pentamethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

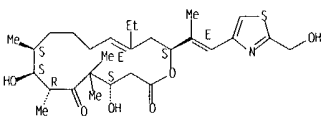
Absolute stereochemistry.
Double bond geometry as described by E or Z.

L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 334934-88-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

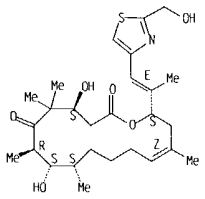
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 334934-97-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,14-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

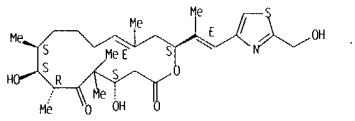
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 20 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 334934-98-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,14-pentamethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

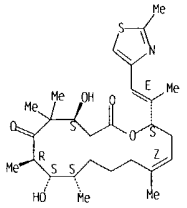
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **189453-10-9P**, Epothilone D
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(assembly of methylthiazolylcarboxy starter unit on EpoB subunit can promote epothilone biosynthesis)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

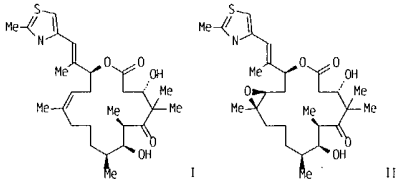
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:686932 CAPLUS
DOCUMENT NUMBER: 136:81944
TITLE: Epothilone biosynthesis: assembly of the methylthiazolylcarboxy starter unit on the EpoB subunit
AUTHOR(S): Chen, H.; O'Connor, S.; Cane, D. E.; Walsh, C. T.
CORPORATE SOURCE: Dep. Biol. Chem. Mol. Pharmacol., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Chemistry & Biology (**2001**), 8(9), 899-912
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Background: Polyketides (PKs) and non-ribosomal peptides (NRPs) are therapeutically important natural products biosynthesized by multimodular protein assembly lines, termed the PK synthases (PKSs) and NRP synthetases (NRPSs), via a similar thiotemplate-mediated mechanism. The potential for productive interaction between these two parallel enzymic systems has recently been demonstrated, with the discovery that PK/NRP hybrid natural products can be of great therapeutic importance. One newly discovered PK/NRP product, epothilone D from Sorangium cellulosum, has shown great potential as an anti-tumor agent. Results: The chain-initiating methylthiazole ring of epothilone has been generated in vitro as an acyl-S-enzyme intermediate, using five domains from two modules of the polymodular epothilone synthetase. The acyl carrier protein (ACP) domain, excised from the EpoA gene, was expressed in Escherichia coli, purified as an apo protein, and then post-translationally primed with acetyl-CoA using the phosphopantetheinyl transferase enzyme Sfp. The four-domain 150-kDa EpoB subunit (cyclization-adenylation-oxidase-peptidyl carrier protein domains: Cy-A-Ox-PCP) was also expressed and purified in soluble form from E. coli. Post-translational modification with Sfp and CoASH introduced the HS-pantP prosthetic group to the apo-PCP, enabling subsequent loading with L-cysteine to generate the Cys-S-PCP acyl enzyme intermediate. When acetyl-S-ACP (EpoA) and cysteinyl-S-EpoB were mixed, the Cy domain of EpoB catalyzed acetyl transfer from EpoA to the amino group of the Cys-S-EpoB, generating a transient N-Ac-Cys-S-EpoB intermediate that is cyclized and dehydrated to the five-membered ring methylthiazolinyl-S-EpoB. Finally, the FMN-containing Ox domain of EpoB oxidized the dihydro heterocyclic thiazolinyl ring to the heteroarom. oxidation state, the methylthiazolylcarboxy-S-EpoB. When other acyl-CoAs were substituted for acetyl-CoA in the Sfp-based priming of the apo-CP domain, addnl. alkylthiazolylcarboxy-S-EpoB acyl enzymes were produced. Conclusions: These expts. establish chain transfer across a PKS and NRPS interface. Transfer of the acetyl group from the ACP domain of EpoA to EpoB reconstitutes the start of the epothilone synthetase assembly line, and installs and converts a cysteine group into a methyl-substituted heterocycle during this natural product chain growth.

L5 ANSWER 22 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:674507 CAPLUS
DOCUMENT NUMBER: 136:37426
TITLE: Chemo- and stereoselective epoxidation of 12,13-desoxyepothilone B using 2,2'-dimethyldioxirane
AUTHOR(S): Stachel, S. J.; Danishefsky, S. J.
CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, The Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Tetrahedron Letters (**2001**), 42(39), 6785-6787
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:37426
GRAPHIC IMAGE:



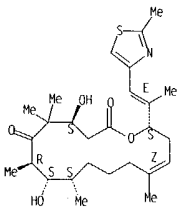
I II

ABSTRACT:
Epoxidn. of 12,13-desoxyepothilone B [dEpoB (I)] to epothilone B [EpoB (II)], using DMDO, reproducibly gives excellent stereoselectivity with high confidence and yield.

IT **189453-10-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(use of 2,2'-dimethyldioxirane for chemo- and stereoselective epoxidn. of 12,13-desoxyepothilone B)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 22 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:661399 CAPLUS
DOCUMENT NUMBER: 135:226826
TITLE: Synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug resistant phenotype
INVENTOR(S): Danishefsky, Samuel J.; Lee, Chul Bom; Chappell, Mark; Stachel, Shawn; Chou, Ting-chao
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 234 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064650	A2	20010907	WO 2001-US6643	20010301 <--
WO 2001064650	A3	20020510		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002058817	A1	20020516	US 2001-796959	20010301
EP 1259490	A2	20021127	EP 2001-916335	20010301
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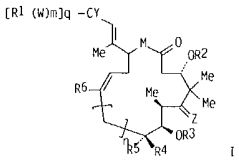
JP 2004500388	T2	20040108	JP 2001-563492	20010301

PRIORITY APPLN. INFO.: US 2000-185968P P 20000301
US 2000-250447P P 20001130
WO 2001-US6643 W 20010301

OTHER SOURCE(S): CASREACT 135:226826; MARPAT 135:226826
GRAPHIC IMAGE:

L5 ANSWER 23 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

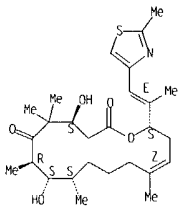
ABSTRACT:
The present invention provides convergent processes for preparing epothilones, desoxyepothilones, and analogs, e.g., I [M = NH, O; CY = aryl, heteroaryl; q = 1-5; W = absent, NH, CO, CS, O, S, C(V)2; V = H, halogen, OH, SH, amino, (un)substituted alkyl, heteroalkyl, aryl, heteroaryl; m = 1-5; bond W···R1 = single bond, double bond; R1 = OR, SR, NR2; CO2R, COR, CONHR, N3, N2, N2R; halogen, un(substituted) cyclic or acyclic aliphatic, heteroaliph., aryl or heteroaryl, polymer, carbohydrate; R = H, un(substituted) cyclic or acyclic aliphatic, heteroaliph., aryl or heteroaryl, protecting group; R2, R3 = H, un(substituted) aliphatic, heteroaliph., aryl, heteroaryl, acyl, aroyl, benzoyl; R4, R5 = H, un(substituted) cyclic or acyclic aliphatic, heteroaliph., aryl or heteroaryl, optionally substituted by one or more of OH, alkoxy, carboxy, carboxaldehyde, N-alkoxyimino, N-alkoxyimino; R6 = H, OR, SR, NR2; CO2R, COR, CONHR, N3, N2, N2R, cyclic acetal, halogen, un(substituted) cyclic or acyclic aliphatic, aryl, heteroaryl; Z = O, N(ORE), NNRFRG; RE, RF, RG = un(substituted) cyclic or acyclic aliphatic; n = 0-3], for the treatment of cancer. Biol. activities of novel compds. based on I and methods for the treatment of cancer and cancer which has developed a multi-drug phenotype are presented. Thus, 21-oxo-12,13-desoxyepothilone B and 15-azaepothilone B were active vs leukemia CCRF-CEM cells (IC50 = 0.027 μM; IC50 = 0.021 μM, resp.).

IT **189453-10-9P**, 12,13-Desoxyepothilone B **198475-07-9P**
252981-50-3P, (-)-12,13-Desoxyepothilone F
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug resistant phenotype)

RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

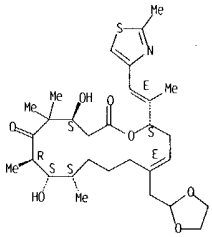
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 23 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-07-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(1,3-dioxolan-2-ylmethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

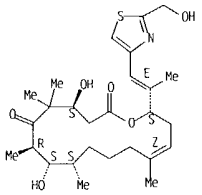
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 252981-50-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 23 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

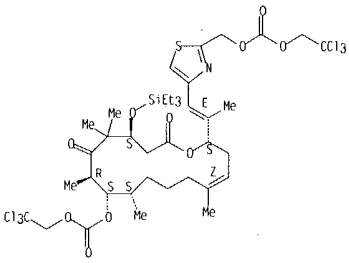


IT **298702-21-3P 298702-22-4P 350493-50-4P**
359014-38-3P 359014-39-4P 359014-40-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug resistant phenotype)

RN 298702-21-3 CAPLUS

CN Carbonic acid, [4-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-5,9,11,13,13-pentamethyl-12,16-dioxo-10-[[(2,2,2-trichloroethoxy)carbonyl]oxy]-14-[(triethylsilyl)oxy]oxacyclohexadec-4-en-2-yl]-1-propenyl]-2-thiazolyl]methyl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

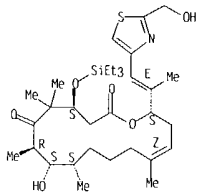


L5 ANSWER 23 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 298702-22-4 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-4-[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

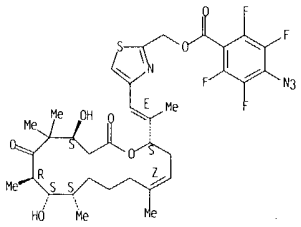
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 350493-50-4 CAPLUS

CN Benzoic acid, 4-azido-2,3,5,6-tetrafluoro-, [4-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-10,14-dihydroxy-5,9,11,13,13-pentamethyl-12,16-dioxooxacyclohexadec-4-en-2-yl]-1-propenyl]-2-thiazolyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

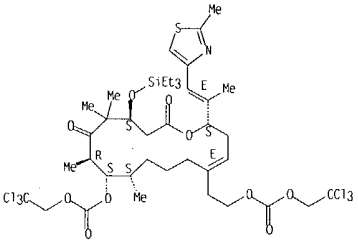


L5 ANSWER 23 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 359014-38-3 CAPLUS

CN Carbonic acid, (4S,7R,8S,9S,13E,16S)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-2,6-dioxo-13-[2-[[(2,2,2-trichloroethoxy)carbonyl]oxy]ethyl]-4-[(triethylsilyl)oxy]oxacyclohexadec-13-en-8-yl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

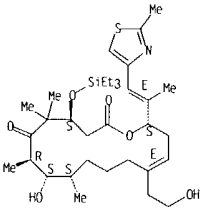
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 359014-39-4 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-13-(2-hydroxyethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13E,16S)- (9Ci) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

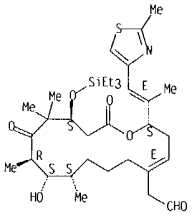


RN 359014-40-7 CAPLUS

L5 ANSWER 23 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CN Oxacyclohexadec-4-ene-5-acetaldehyde, 10-hydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-14-[(triethylsilyl)oxy]-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

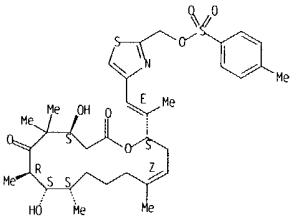


IT **359014-45-2P 359417-21-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug resistant phenotype)

RN 359014-45-2 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-[2-[[[(4-methylphenyl)sulfonyl]oxy]methyl]-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

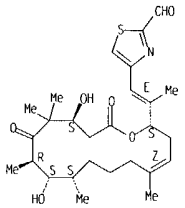


RN 359417-21-3 CAPLUS

CN 2-Thiazolecarboxaldehyde, 4-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-10,14-

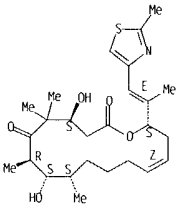
L5 ANSWER 23 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
dihydroxy-5,9,11,13,13-pentamethyl-12,16-dioxooxacyclohexadec-4-en-2-yl]-1-propenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



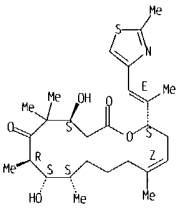
L5 ANSWER 24 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 24 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:658077 CAPLUS
DOCUMENT NUMBER: 135:205580
TITLE: Method for inhibiting or treating chemotherapy-induced hair loss
INVENTOR(S): Atwal, Karnail S.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S. Ser. No. 447,002.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001020038	A1	20010906	US 2001-805347	20010313 <--
US 6458835	B2	20021001		
US 6013668	A	20000111	US 1998-119884	19980721 <--
ZA 9807220	A	20000214	ZA 1998-7220	19980812 <--
US 6472427	B1	20021029	US 1999-447002	19991122
US 6262122	B1	20010717	US 2000-615345	20000712 <--

PRIORITY APPLN. INFO.: US 1997-55568P P 19970813
US 1998-71364P P 19980115
US 1998-119884 A1 19980721
US 1999-447002 A2 19991122

ABSTRACT:
A method for inhibiting hair loss and/or promoting hair growth in chemotherapy and/or radiation therapy patients wherein the (R)-enantiomer of 4-[[(cyanoimino)-[(1,2,2-trimethylpropyl)amino]methyl]amino]benzonitrile is administered prior to, simultaneous with and/or after chemotherapy and/or radiation treatment. There was a remarkable difference between the 1-(R)-enantiomer and the 2-(S)enantiomer in their effect on hair follicle stimulation; in particular the (R)-enantiomer had a faster onset of action compared to the corresponding (S)-enantiomer. While the IC50 for vasorelaxant potency of the (R)-enantiomer is 47±17 nM vs. 157±35 nM for the (S)-enantiomer, the hair growth promoting ability of the (R)-enantiomer for producing hair growth within 11 days of treatment is 8 times greater than the corresponding (S)-enantiomer.

IT **186692-73-9**, Epothilone C **189453-10-9**, Epothilone D
RL: AOV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor; method for inhibiting or treating chemotherapy-induced hair loss)
RN 186692-73-9 CAPLUS

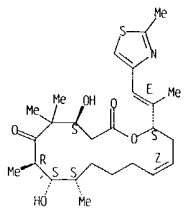
L5 ANSWER 25 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:603086 CAPLUS
DOCUMENT NUMBER: 136:47797
TITLE: Recent developments in the chemistry, biology and medicine of the epothilones
AUTHOR(S): Nicolaou, K. C.; Ritzen, Andreas; Namoto, Kenji
CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Chemical Communications (Cambridge, United Kingdom) (2001), (17), 1523-1535
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

ABSTRACT:
A review. The epothilones have occupied center stage on the scenes of total synthesis, chemical biol. and medicine for the last five years, no doubt because of their intriguing mode of action and unusually high potency against tumor cells, including multidrug-resistant cell lines. This article reviews the most recent advances within this exciting field. Thus, an overview of recent synthetic endeavors culminating in a new generation of total syntheses and analogs, some with higher potencies than the naturally occurring substances, will be given, and the chemical biol., in particular the current understanding of structure-activity relationships of the epothilones, will also be discussed in light of the latest biol. results. In addition, the recently elucidated biosynthetic machinery of the natural epothilone-producing myxobacterium Sorangium cellulosum, as it is now understood, will be described. Finally, some preclin. and clin. studies will be summarized.

IT **186692-73-9DP**, Epothilone c, analogs
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chemical, biol, and medicine of epothilones)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 25 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 26 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

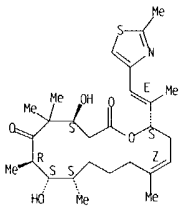
ACCESSION NUMBER: 2001:552436 CAPLUS
DOCUMENT NUMBER: 135:352420
TITLE: Selective potentiation of paclitaxel (Taxol)-induced cell death by mitogen-activated protein kinase kinase inhibition in human cancer cell lines
AUTHOR(S): McDaid, Hayley M.; Horwitz, Susan Band
CORPORATE SOURCE: Department of Molecular Pharmacology, Albert Einstein College of Medicine, Bronx, NY, USA
SOURCE: Molecular Pharmacology (2001), 60(2), 290-301
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:

Activation of the mitogen-activated protein kinase (MAPK) pathway in HeLa and Chinese hamster ovary cells after treatment with paclitaxel (Taxol) and other microtubule interacting agents has been investigated. Using a trans-reporting system, the phosphorylation of the nuclear transcription factors Elk-1 and c-jun was measured. Concentration- and time-dependent activation of the Elk-1 pathway, mediated primarily by the extracellular signal-regulated kinase (ERK) component of the MAPK family, was observed. Inactive drug analogs and other cytotoxic compds. that do not target microtubules failed to induce similar levels of activation, thereby indicating that an interaction between these drugs and the microtubule is essential for the activation of MAPKs. Evaluation of the endogenous levels of MAPK expression revealed cell-dependent expression of the ERK, c-jun N-terminal kinase, and p38 pathways. In the case of HeLa cells, time-dependent activation of ERK coincided with increased poly(ADP-ribose) polymerase (PARP) cleavage, phosphatidylserine externalization, and increased accumulation of cells in G2M. In both cell lines, inhibition of ERK activity potentiated paclitaxel-induced PARP cleavage and phosphatidylserine externalization, suggesting that ERK activity coincided with, but did not mediate, the cytotoxic effects of paclitaxel. We evaluated the nature of the interaction between paclitaxel and the MAPK kinase inhibitor U0126 in three cell lines, on the basis of a potential chemotherapeutic advantage of paclitaxel plus ERK inhibition. Our data confirmed additivity in those cells lines that undergo paclitaxel-induced ERK activation, and antagonism in cells with low ERK activity, suggesting that in tumors with high ERK activity, there may be an application for this strategy in therapy.

IT **189453-10-9**, Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effect of paclitaxel and other microtubule interacting substances on the MAPK pathway in human cancer cell lines)
RN 189453-10-9 CAPLUS

L5 ANSWER 26 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

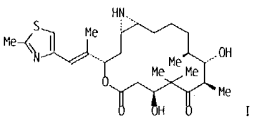
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 27 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:538367 CAPLUS
DOCUMENT NUMBER: 135:272779
TITLE: Synthesis and Biological Activity of Novel Epothilone Aziridines
AUTHOR(S): Regueiro-Ren, Alicia; Borzilleri, Robert M.; Zheng, Xiaoping; Kim, Soong-Hoon; Johnson, James A.; Fairchild, Craig R.; Lee, Francis Y. F.; Long, Byron H.; Vite, Gregory D.
CORPORATE SOURCE: Divisions of Discovery Chemistry and Oncology Drug Discovery, The Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543-4000, USA
SOURCE: Organic Letters (2001), 3(17), 2693-2696
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:272779
GRAPHIC IMAGE:



I

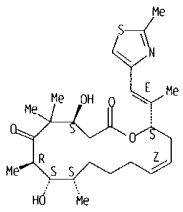
ABSTRACT:

A series of 12α,13α-aziridinyl epothilone derivs., e.g. I, were synthesized in an efficient manner from epothilone A. The final semisynthetic route involves a formal double-inversion of stereochem. at both the C12 and C13 positions. All aziridine analogs were tested for effects on tubulin binding polymerization and cytotoxicity. The results indicate that the aziridine moiety is a viable isosteric replacement for the epoxide in the case of epothilones.

IT **186692-73-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and biol. activity of novel epothilone aziridines)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 27 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



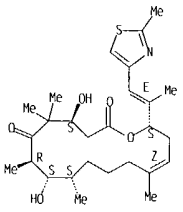
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 28 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
B and F against human tumor xenografts in nude mice)

RN 189453-10-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

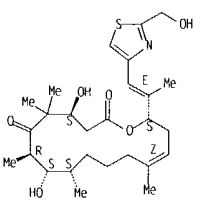
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 252981-50-3 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 28 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:526491 CAPLUS
DOCUMENT NUMBER: 135:327022
TITLE: The synthesis, discovery, and development of a highly promising class of microtubule stabilization agents: curative effects of desoxyepothilones B and F against human tumor xenografts in nude mice
AUTHOR(S): Chou, Ting-Chao; O'Connor, Owen A.; Tong, William P.; Guan, Yongbiao; Zhang, Zui-Guo; Stachel, Shawn J.; Lee, Chulbom; Danishefsky, Samuel J.
CORPORATE SOURCE: Preclinical Pharmacology Core Facility, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(14), 8113-8118
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
We have evaluated two synthetic epothilone analogs lacking the 12,13-epoxide functionality, 12,13-desoxyepothilone B (dEpoB), and 12,13-desoxyepothilone F (dEpoF). The concns. required for 50% growth inhibition (IC50) for a variety of anticancer agents were measured in CCRF-CEM/VBL1000 cells (2,048-fold resistance to vinblastine). By using dEpoB, dEpoF, aza-EpoB, and paclitaxel, the IC50 values were 0.029, 0.092, 2.99, and 5.17 μM, resp. These values represent 4-, 33.5-, 1.423-, and 3.133-fold resistance, resp., when compared with the corresponding IC50 in the parent [nonmultiple drug-resistant (MDR)] CCRF-CEM cells. We then produced MDR human lung carcinoma A549 cells by continuous exposure of the tumor cells to sublethal concns. of dEpoB (1.8 yr), vinblastine (1.2 yr), and paclitaxel (1.8 yr). This continued exposure led to the development of 2.1-, 4.848-, and 2.553-fold resistance to each drug, resp. The therapeutic effect of dEpoB and paclitaxel was also compared in vivo in a mouse model by using various tumor xenografts. DEpoB is much more effective in reducing tumor sizes in all MDR tumors tested. Anal. of dEpoF, an analog possessing greater aqueous solubility than dEpoB, showed curative effects similar to dEpoB against K562, CCRF-CEM, and MX-1 xenografts. These results indicate that dEpoB and dEpoF are efficacious antitumor agents with both a broad chemotherapeutic spectrum and wide safety margins.

IT **189453-10-9**, Desoxyepothilone B **252981-50-3**, Desoxyepothilone F
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(curative effects of microtubule stabilization agents desoxyepothilones

L5 ANSWER 29 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:431121 CAPLUS
DOCUMENT NUMBER: 135:235792
TITLE: Epothilones and their analogues - a new class of promising microtubule inhibitors
AUTHOR(S): Florsheimer, Andreas; Altmann, Karl-Heinz
CORPORATE SOURCE: TA Oncology Research and Corporate Research, Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Expert Opinion on Therapeutic Patents (2001), 11(6), 951-968
CODEN: EOTPEG; ISSN: 1354-3776
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with 134 refs. Epothilones A and B are naturally occurring microtubule depolymn. inhibitors, which inhibit the growth of human cancer cells in vitro at nanomolar or even sub-nanomolar concns. In contrast to paclitaxel (Taxol, Bristol-Myers Squibb) epothilones are also active against multi-drug resistant cancer cell lines and epothilone B exhibits potent in vivo antitumor activity against multidrug-resistant tumors. In addition, epothilones A and B have been shown to be active in vitro against cell lines whose paclitaxel-resistance is derived from specific tubulin mutations. Their attractive preclin. profile has made epothilones important lead structures in the search for improved cytotoxic anticancer drugs and hundreds of analogs and derivs. of epothilones have been prepared and biol. characterized over the past four years. While chemical modifications have been reported for almost every position of the epothilone structural framework, the major focus has been on modifications of the epoxide moiety at C-12/C-13, the C-6-position, the ester linkage and the unsatd. heterocyclic side-chain. Several of the compds. thus produced exhibit low nM IC50 values for the inhibition of human cancer cell proliferation and may represent potential development candidates. Currently, two compds., natural epothilone B and BMS247550, the lactam analog of epothilone B, are undergoing clin. trials. An addnl. analog, epothilone D, also known as deoxyepothilone B, appears to be in late stage preclin. development and may enter clin. trials in the near future.

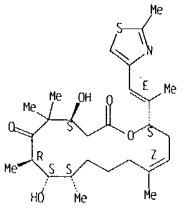
IT **189453-10-9**, Epothilone d
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epothilones and analogs as new class of promising microtubule inhibitors)

RN 189453-10-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

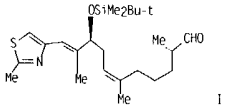
L5 ANSWER 29 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 30 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:421797 CAPLUS
DOCUMENT NUMBER: 135:180642
TITLE: Total Synthesis of Epothilones B and D
AUTHOR(S): Taylor, Richard E.; Chen, Yue
CORPORATE SOURCE: Department of Chemistry & Biochemistry, University of Notre Dame, Notre Dame, IN, 46556-5670, USA
SOURCE: Organic Letters (2001), 3(14), 2221-2224
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:180642
GRAPHIC IMAGE:



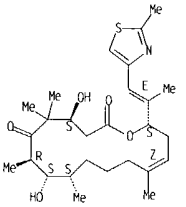
I

ABSTRACT:
A highly convergent total synthesis of the natural products epothilone B and D is described. The route is highlighted by efficient generation of a C12-C13 trisubstituted olefin I which exploits a sequential Nozaki-Hiyama-Kishi coupling and a stereoselective thionyl chloride rearrangement.

IT **189453-10-9P**, Epothilone D **189453-35-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of macrolides epothilone B and D)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

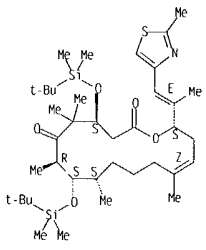
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 30 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

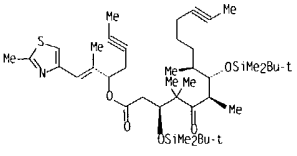
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 31 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:415950 CAPLUS
DOCUMENT NUMBER: 135:242035
TITLE: Concise total syntheses of epothilone A and C based on alkyne metathesis
AUTHOR(S): Furstner, Alois; Mathes, Christian; Grela, Karol
CORPORATE SOURCE: Max-Planck-Institut fur Kohlenforschung, Mulheim/Ruhr, D-45466, Germany
SOURCE: Chemical Communications (Cambridge, United Kingdom) (2001), (12), 1057-1059
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:242035
GRAPHIC IMAGE:



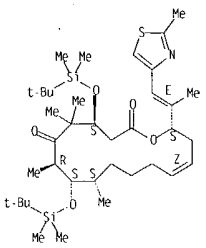
I

ABSTRACT:
A ring closing alkyne metathesis reaction of I catalyzed by a molybdenum complex followed by a Lindlar reduction of the resulting cycloalkyne product opens an efficient and stereoselective entry into epothilone A and C.

IT **186692-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(concise total syntheses of epothilone A and C based on alkyne metathesis)
RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

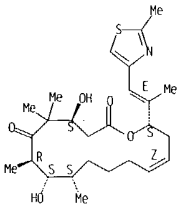
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 31 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **186692-73-9P**, Epothilone C
RL: SPN (Synthetic preparation); PREP (Preparation)
(concise total syntheses of epothilone A and C based on alkyne metathesis)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

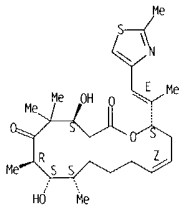
L5 ANSWER 32 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:413810 CAPLUS
DOCUMENT NUMBER: 135:179755
TITLE: New Natural Epothilones from Sorangium cellulosum, Strains So ce90/B2 and So ce90/D13: Isolation, Structure Elucidation, and SAR Studies
AUTHOR(S): Hardt, Ingo H.; Steinmetz, Heinrich; Gerth, Klaus; Sasse, F.; Reichenbach, Hans; Hoefle, Gerhard
CORPORATE SOURCE: Gesellschaft fuer Biotechnologische Forschung mbH, Braunschweig, D-38124, Germany
SOURCE: Journal of Natural Products (2001), 64(7), 847-856
CODEN: JNPRDF; ISSN: 0163-3864
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
In addition to epothilones A (1) and B (2), 37 natural epothilone variants and epothilone-related compds. were isolated from the culture broth of a 700 L fermentation of Sorangium cellulosum, strain So ce90/B2. Of these, only the 12,13-desoxyepothilones, epothilone C (14) and D (15), were produced in significant amts. (3-6 mg/L); the 21-hydroxy derivs. and epothilones E (3) and F (4), in low and variable amts. due to further degradation by the producing organism. Most of the other epothilone variants were produced only in 1-100 μg/L amts. The new compds. are very similar in structure to the parent compds. 1, 2 and 14, 15 and are presumably the result of the imperfect selectivity of the biosynthetic enzymes for acetate and propionate. Further, epothilones containing an oxazole moiety (10-13) in the side chain instead of a thiazole as well as ring-expanded 18-membered macrolides, epothilones I (30-35), and a ring contracted 14-membered macrolide, epothilone K (36), were found as very minor metabolites. The mutant strain, So ce90/D13, instead of macrolactones, produced short-chain carboxylic acids 40, 41, and 42 bearing the characteristic thiazole side chain. The structures of the new epothilones were elucidated on the basis of comprehensive NMR and MS data. The new epothilone variants were tested in a cytotoxicity assay with mouse fibroblasts (cell line L929), and structure-activity relationships were established. Several new natural epothilones showed activity comparable to 1 and 2, but in no case exceeded that of 2.

IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
192370-82-4P, Epothilone C4 **198475-12-6P**, Epothilone H1
198571-09-4P, Epothilone H2 **252917-44-5P**, Epothilone C7
252917-46-7P, Epothilone C8 **252917-47-8P**, Epothilone C9
RL: BPN (Biosynthetic preparation); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(new natural epothilones from Sorangium cellulosum)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

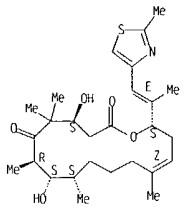
L5 ANSWER 31 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L5 ANSWER 32 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

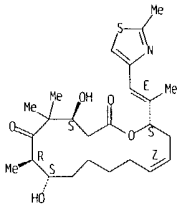
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 192370-82-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

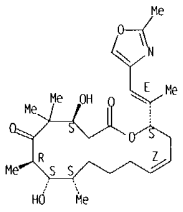
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 32 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

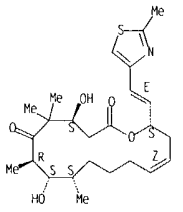
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-09-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

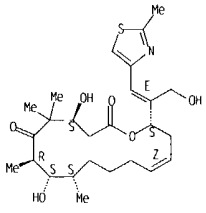
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 32 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



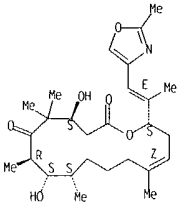
RN 252917-47-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-1-(hydroxymethyl)-2-(2-methyl-4-thiazolyl)ethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



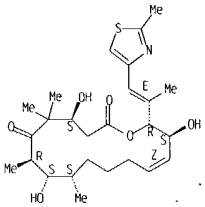
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 32 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 252917-44-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8,15-trihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,15S,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

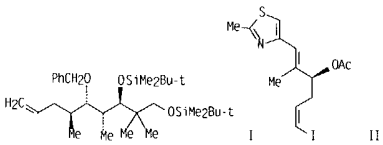


RN 252917-46-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 33 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:361612 CAPLUS
DOCUMENT NUMBER: 135:137326
TITLE: Methodology based on chiral silanes in the synthesis of polypropionate-derived natural products - total synthesis of epothilone A
AUTHOR(S): Zhu, Bin; Panek, James S.
CORPORATE SOURCE: R. W. Johnson Pharmaceutical Research Institute, Raritan, NJ, 08869, USA
SOURCE: European Journal of Organic Chemistry (2001), (9), 1701-1714
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:137326
GRAPHIC IMAGE:

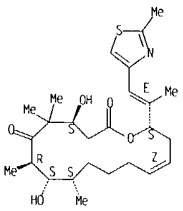


ABSTRACT:
Epothilones A and B are natural products with potent antitumor activity. These compds. have a Taxol-like mechanism of action against tumor cells. A total synthesis of epothilone A is reported, which is based on the synthesis and union of two advanced fragments: C3-C11 fragment I and C12-C21 fragment II. Bond construction methodol. based on chiral silanes was utilized to introduce the key C6 and C7 stereocenters of fragment I. A lipase-mediated kinetic resolution established the C15 stereocenter of fragment II. The 16-membered lactone was constructed using a three-step sequence: an intermol. B-alkyl Suzuki coupling of I and II, an aldol condensation, and a Yamaguchi-type macrolactonization reaction.

IT **186692-73-9P 187283-49-4P 297131-86-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(methodol. based on chiral silanes in synthesis of polypropionate-derived natural products, total synthesis of epothilone A)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

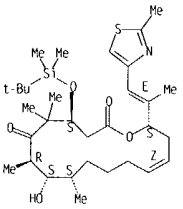
L5 ANSWER 33 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 187283-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

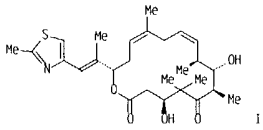
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 297131-86-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-8-(phenylmethoxy)-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 34 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2001:347752 CAPLUS
DOCUMENT NUMBER:	135:107176
TITLE:	Total Synthesis of Epothilone B, Epothilone D, and cis- and trans-9,10-Dehydroepothilone D
AUTHOR(S):	White, James D.; Carter, Rich G.; Sundermann, Kurt F.; Wartmann, Markus
CORPORATE SOURCE:	Department of Chemistry, Oregon State University, Oregon, OR, 97331-4003, USA
SOURCE:	Journal of the American Chemical Society (2001), 123(23), 5407-5413 CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 135:107176
GRAPHIC IMAGE:	

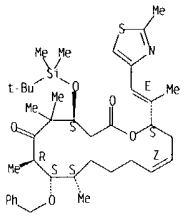


I

ABSTRACT:
Cis-9,10-dehydroepothilone D (I) was prepared via Wittig reaction, and was selectively reduced with diimide to yield epothilone D and, after epoxidn., epothilone B. An alternative route to epothilone D employed a Castro-Stephens reaction. Trans-9,10-dehydroepothilone D (II) was prepared via a Stille coupling. Bioassay data comparing the antiproliferative activity and tubulin polymerization of I and II with epothilone B, epothilone D, and paclitaxel showed that the synthetic analogs were less potent than their natural counterparts, although both retain full antiproliferative activity against a paclitaxel-resistant cell line. No significant difference in potency was noted between cis analog I and its trans isomer II.

IT **189453-10-9P**, Epothilone D
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis, antitumor activity and tubulin polymerization of epothilone B, epothilone D, and cis- and trans-9,10-dehydroepothilone D)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

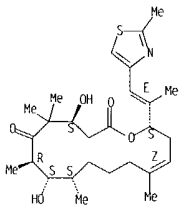
L5 ANSWER 33 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 34 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



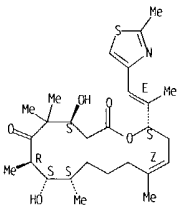
REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 35 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:334742 CAPLUS
DOCUMENT NUMBER: 135:107175
TITLE: On the Interactivity of Complex Synthesis and Tumor Pharmacology in the Drug Discovery Process: Total Synthesis and Comparative in Vivo Evaluations of the 15-Aza Epothilones
AUTHOR(S): Stachel, Shawn J.; Lee, Chul Bom; Spassova, Maria; Chappell, Mark D.; Bornmann, William G.; Danishefsky, Samuel J.; Chou, Ting-Chao; Guan, Yongbiao
CORPORATE SOURCE: Laboratories for Bioorganic Chemistry Preclinical Pharmacology and the Preparative Synthesis Core Facility, The Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Journal of Organic Chemistry (2001), 66(12), 4369-4378
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:107175
ABSTRACT:
The total syntheses of 12,13,15-desoxy-15(S)-aza-epothilone B (aza-dEpoB; dEpoB-lactam) and 12,13,15-desoxy-15(R)-aza-epothilone B (15-epi-aza-dEpoB; 15-epi-dEpoB-lactam) have been accomplished via a highly convergent strategy. We have also successfully oxidized 12,13,15-desoxy-15(S)-aza-epothilone B to aza-epothilone B (aza-EpoB; EpoB-lactam). Aza-epothilone B has been advanced to phase I clin. trials by the Bristol-Myers Squibb group. Our synthesis is efficient and was amenable to the production of significant quantities of these lactams. Using our fully synthetically derived lactams, in vitro and in vivo studies were conducted in comparison with advanced clin. candidates. 12,13-desoxyepothilone B and 12,13-desoxyepothilone F, also derived by total synthesis.

IT **189453-10-9**, 12,13-Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antitumor evaluation of)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

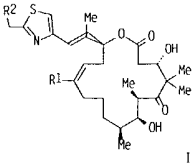
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 35 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 36 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:332215 CAPLUS
DOCUMENT NUMBER: 135:107166
TITLE: Insights into Long-Range Structural Effects on the Stereochemistry of Aldol Condensations: A Practical Total Synthesis of Desoxyepothilone F
AUTHOR(S): Lee, Chul Bom; Wu, Zhicai; Zhang, Fei; Chappell, Mark D.; Stachel, Shawn J.; Chou, Ting-Chao; Guan, Yongbiao; Danishefsky, Samuel J.
CORPORATE SOURCE: The Laboratories for Bioorganic Chemistry and Preclinical Pharmacology, The Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Journal of the American Chemical Society (2001), 123(22), 5249-5259
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:107166
GRAPHIC IMAGE:



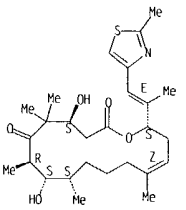
I

ABSTRACT:
A processable total synthesis of a potent antitumor agent, desoxyepothilone F [dEpoF, 21-hydroxy-12,13-desoxyepothilone B, 21-hydroxyepothilone D (I; R1 = Me, R2 = OH)], has been accomplished. The route is highly convergent. The new technol. has also been applied to a total synthesis of 12,13-desoxyepothilone B [dEpoB (I; R1 = Me, R2 = H)]. The crucial point of departure from previous syntheses of I (R1 = Me, R2 = H, OH) involves presentation of the C1-C11 sector for Suzuki coupling with C3 in reduced form. Hitherto, the required S stereochem. at C3 had been implemented via reduction of a keto function after Suzuki coupling. Whereas that chemical worked quite well in a synthesis of I (R1 = Me, R2 = H), it was not transferable to a high-yielding synthesis of I (R1 = Me, R2 = OH). The reduction of the keto group at C3 via a Noyori protocol after Suzuki coupling had proved to be very difficult. In our current approach, two consecutive aldol reactions are used to fashion the acyl sector. In the first

L5 ANSWER 36 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
aldol condensation, C6 becomes attached to C7. Following protection at C7, a two-carbon acetate equiv. is used to join C2 and C3 with very high asym. induction at C3. Only after this center has been implemented is the Suzuki reaction conducted. This major advance allowed us to synthesize I (R1 = Me, R2 = OH) in a straightforward fashion. These findings found ready application in the total synthesis of dEpoB. Another part of the study involved anal. of the factors assocd. with aldol condensations joining C6 to C7. In the work described herein, the consequences of the status of C3 in promoting the C6-C7 aldol coupling are probed in detail. Dramatic stereochem. long-range effects uncovered during the study are described, and a working model to explain these effects has emerged.

IT **189453-10-9P**, Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
(total synthesis of desoxyepothilone F via two consecutive aldol condensations and a Suzuki coupling)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

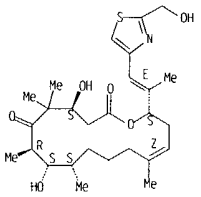
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **252981-50-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of desoxyepothilone F via two consecutive aldol condensations and a Suzuki coupling)
RN 252981-50-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 36 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

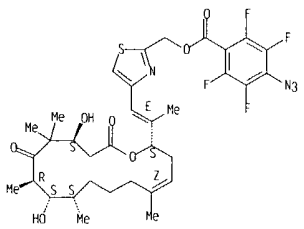
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **350493-50-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(total synthesis of desoxyepothilone F via two consecutive aldol condensations and a Suzuki coupling)
RN 350493-50-4 CAPLUS
CN Benzoic acid, 4-azido-2,3,5,6-tetrafluoro-, [4-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-10,14-dihydroxy-5,9,11,13,13-pentamethyl-12,16-dioxooxacyclohexadec-4-en-2-yl]-1-propenyl]-2-thiazolyl]methyl ester (9CI) (CA INDEX NAME)

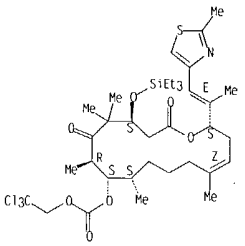
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 36 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **241129-40-8P**
RL: PNU (Preparation, unclassified); PREP (Preparation)
(total synthesis of desoxyepothilone F via two consecutive aldol condensations and a Suzuki coupling)
RN 241129-40-8 CAPLUS
CN Carbonic acid, (4S,7R,8S,9S,13Z,16S)-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-2,6-dioxo-4-[(triethylsilyl)oxy]oxacyclohexadec-13-en-8-yl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

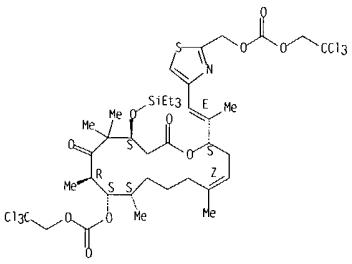
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 36 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **298702-21-3P 298702-22-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of desoxyepothilone F via two consecutive aldol condensations and a Suzuki coupling)
RN 298702-21-3 CAPLUS
CN Carbonic acid, [4-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-5,9,11,13,13-pentamethyl-12,16-dioxo-10-[[(2,2,2-trichloroethoxy)carbonyl]oxy]-14-[(triethylsilyl)oxy]oxacyclohexadec-4-en-2-yl]-1-propenyl]-2-thiazolyl]methyl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

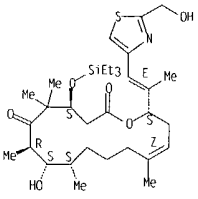
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 298702-22-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-4-[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

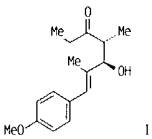
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 36 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

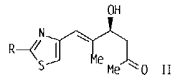


REFERENCE COUNT: 114 THERE ARE 114 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 37 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:316603 CAPLUS
DOCUMENT NUMBER: 135:76707
TITLE: Catalytic antibody route to the naturally occurring epothilones: total synthesis of epothilones A - F
AUTHOR(S): Sinha, Subhash C.; Sun, Jian; Miller, Gregory P.; Wartmann, Markus; Lerner, Richard A.
CORPORATE SOURCE: Department of Molecular Biology and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Chemistry--A European Journal (2001), 7(8), 1691-1702
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:76707
GRAPHIC IMAGE:



I



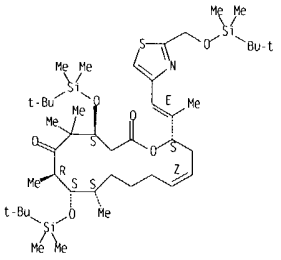
II

ABSTRACT:
Naturally occurring epothilones have been synthesized starting from enantiomerically pure aldol compds. I and II, which were obtained by antibody catalysis. Aldolase antibody 38C2 catalyzed the resolution of (±)-I by enantioselective retro-aldol reaction to afford I in 90% ee at 50% conversion. Compds. I' (R = Me, CH2OH) were obtained in more than 99% ee at 50% conversion by resolution of their racemic mixts. using newly developed aldolase antibodies 84G3, 85H6 or 93F3. Compds. I and II were resolved in multigram quantities and then converted to the epothilones by metathesis processes, which were catalyzed by Grubbs' catalysts.

IT **346652-75-3P**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

L5 ANSWER 37 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-[2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

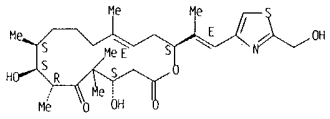


RN 346652-33-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-[2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

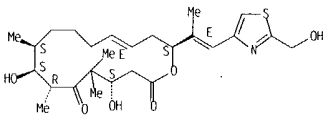
L5 ANSWER 37 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(total synthesis of epothilones A-F)
RN 346652-75-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



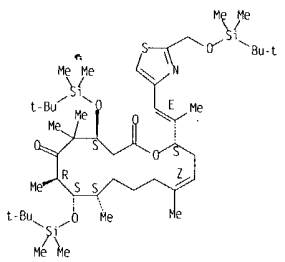
IT **204513-14-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(total synthesis of epothilones A-F)
RN 204513-14-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



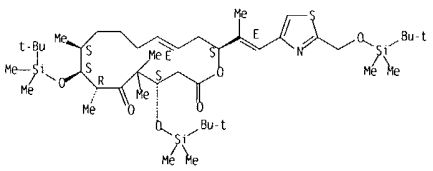
IT **346652-29-7P 346652-33-3P 346652-69-5P**
346652-70-8P
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of epothilones A-F)
RN 346652-29-7 CAPLUS

L5 ANSWER 37 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 346652-69-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-[2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

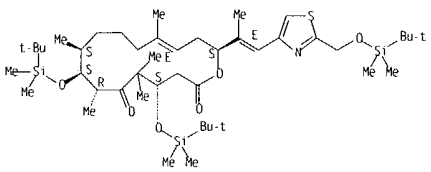
Absolute stereochemistry.
Double bond geometry as shown.



RN 346652-70-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-[2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

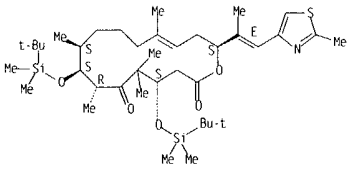
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 37 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **204195-20-0P**
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(total synthesis of epothilones A-F)
RN 204195-20-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

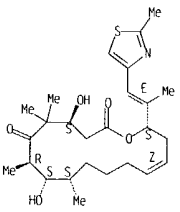
Absolute stereochemistry.
Double bond geometry as described by E or Z.



IT **252981-50-3P**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of epothilones A-F via aldolase antibody catalyzed retro-aldol reaction)
RN 252981-50-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-

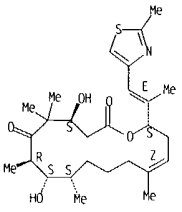
L5 ANSWER 37 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: PNU (Preparation, unclassified); PREP (Preparation)
(total synthesis of epothilones A-F via aldolase antibody catalyzed retro-aldol reaction)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

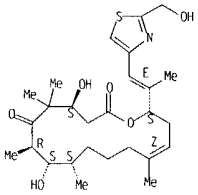
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 117 THERE ARE 117 CITED REFERENCES AVAILABLE FOR

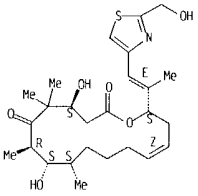
L5 ANSWER 37 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **204513-12-2P**
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(total synthesis of epothilones A-F via aldolase antibody catalyzed retro-aldol reaction)
RN 204513-12-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 37 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 38 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:284132 CAPLUS
DOCUMENT NUMBER: 134:311033
TITLE: Synthesis and biological activity of 13-alkyl epothilone derivatives
INVENTOR(S): Sinha, Subhash C.; Lerner, Richard A.; Barbas, Carlos F.; Sun, Jian
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Scripps Research Institute
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027308	A2	20010419	WO 2000-EP9817	20001006 <--
WO 2001027308	A3	20011213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6294374	B1	20010925	US 1999-415453	19991008 <--
EP 1224316	A2	20020724	EP 2000-966129	20001006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-415453 A 19991008
US 2000-213064P P 20000621
WO 2000-EP9817 W 20001006
OTHER SOURCE(S): CASREACT 134:311033; MARPAT 134:311033
GRAPHIC IMAGE:

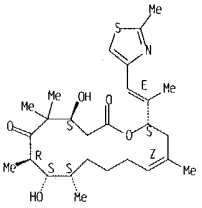
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
The 13-lower alkyl epothilones I (R1 = Me, hydroxymethyl, halomethyl, SMe or OMe; R2 = H or Me, R3 = lower alkyl, and Z = O, bond) were prepared as antitumor agents and a process for enantioselectively resolving a racemic mixture of aldol synthons by means of antibody catalyzed retro-aldol reaction has been developed. Thus, the (-)-thiazole II, obtained by resoln. of the racemic compd. using antibody 84G3, was silylated, followed by methylenylation, desilylation and condensation with acid III and then cyclization in presence of Grubbs catalyst to give epothilone derivs. IV and V. The IC50 for KB-31 tumor cell growth inhibition of IV was 150 nM.

IT **253447-39-1P 253447-56-2P 253447-71-1P**
253447-83-5P 334934-75-7P 334934-76-8P
334934-81-5P 334934-82-6P 334934-87-1P
334934-88-2P
RL: BAC (Biological activity or effector, except adverse); BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and biol. evaluation of 13-alkyl epothilone derivs.)

RN 253447-39-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

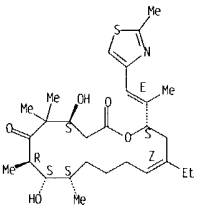
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 253447-56-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

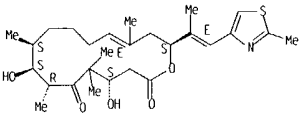
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 38 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



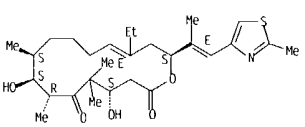
RN 253447-71-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 253447-83-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

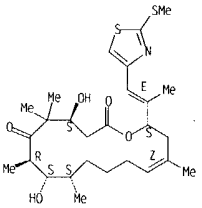
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 334934-75-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-

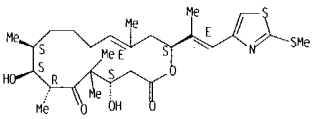
L5 ANSWER 38 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 334934-76-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

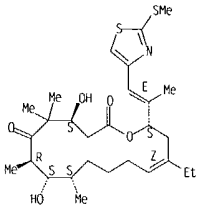
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 334934-81-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

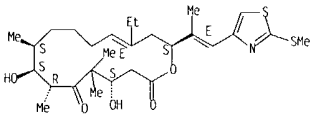
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 38 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 334934-82-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

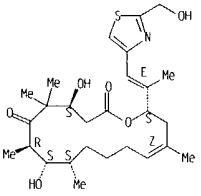
Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 334934-87-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

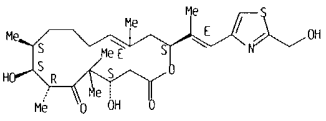
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 38 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

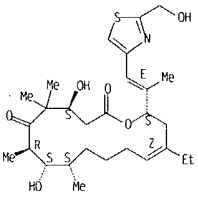


RN 334934-98-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,14-pentamethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.

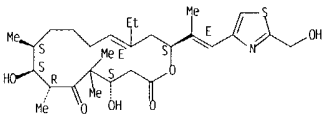


L5 ANSWER 38 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 334934-88-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



IT **334934-97-3P 334934-98-4P**
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and biol. evaluation of 13-alkyl epothilone derivs.)
RN 334934-97-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,14-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 39 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:283821 CAPLUS
DOCUMENT NUMBER: 134:316086
TITLE: Manufacture of polyglutamate-therapeutic agent conjugates
INVENTOR(S): Kumar, Anil M.; Klein, J. Peter; Bhatt, Rama; Vawter, Edward
PATENT ASSIGNEE(S): Cell Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001026693	A2	20010419	WO 2000-US28109	20001012 <--
WO 2001026693	A3	20011227		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1225917	A2	20020731	EP 2000-972079	20001012
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003511423	T2	20030325	JP 2001-529754	20001012
BR 2000014652	A	20030610	BR 2000-14652	20001012
NO 2002001701	A	20020523	NO 2002-1701	20020411
NZ 529789	A	20031219	NZ 2003-529789	20031126

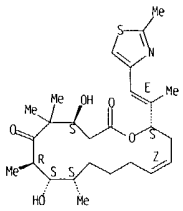
PRIORITY APPLN. INFO.: US 1999-159135P P 19991012
WO 2000-US28109 W 20001012

ABSTRACT:
The invention provides new processes for preparing polyglutamic acid-therapeutic agent conjugates for clin. development and pharmaceutical use, and polyglutamic acid-therapeutic agent conjugates prepared by these processes. Poly(L-glutamic acid) in N,N-dimethylformamide was reacted with paclitaxel in presence of N,N-diisopropylcarbodiimide to obtain poly-L-glutamic acid-2'-paclitaxel conjugate.

IT **186692-73-9DP**, Epothilone c, conjugates **189453-10-9DP**, Epothilone d, conjugates
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(manufacture of polyglutamate-therapeutic agent conjugates)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-

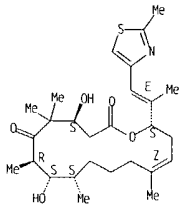
L5 ANSWER 39 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13Z.16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9.13-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13Z.16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 40 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:265220 CAPLUS
DOCUMENT NUMBER: 134:290397
TITLE: Compositions and methods for treating cancer using immunoconjugates and chemotherapeutic agents
INVENTOR(S): Chari. Ravi V. J.
PATENT ASSIGNEE(S): Immunogen. Inc.. USA
SOURCE: PCT Int. Appl.. 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001024763	A2	20010412	WO 2000-US26800	20000929 <--
WO 2001024763	A3	20011011		
W: AE. AG. AL. AM. AT. AU. AZ. BA. BB. BG. BR. BY. BZ. CA. CH. CN. CR. CU. CZ. DE. DK. DM. DZ. EE. ES. FI. GB. GD. GE. GH. GM. HR. HU. ID. IL. IN. IS. JP. KE. KG. KP. KR. KZ. LC. LK. LR. LS. LT. LU. LV. MA. MD. MG. MK. MN. MW. MX. MZ. NO. NZ. PL. PT. RO. RU. SD. SE. SG. SI. SK. SL. TJ. TM. TR. TT. TZ. UA. UG. US. UZ. VN. YU. ZA. ZW. AM. AZ. BY. KG. KZ. MD. RU. TJ. TM				
RW: GH. GM. KE. LS. MW. MZ. SD. SL. SZ. TZ. UG. ZW. AT. BE. CH. CY. DE. DK. ES. FI. FR. GB. GR. IE. IT. LU. MC. NL. PT. SE. BF. BJ. CF. CG. CI. CM. GA. GN. GW. ML. MR. NE. SN. TD. TG				
AU 2000079885	A5	20010510	AU 2000-79885	20000929 <--
EP 1229934	A2	20020814	EP 2000-970516	20000929
R: AT. BE. CH. DE. DK. ES. FR. GB. GR. IT. LI. LU. NL. SE. MC. PT. IE. SI. LT. LV. FI. RO. MK. CY. AL				
JP 2003528034	T2	20030924	JP 2001-527762	20000929

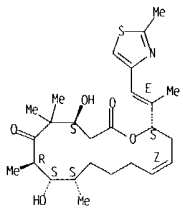
PRIORITY APPLN. INFO.: US 1999-157051P P 19991001
WO 2000-US26800 W 20000929

ABSTRACT:
The present invention is based on the discovery that the administration of at least one immunoconjugate and at least one chemotherapeutic agent provides an unexpectedly superior treatment for cancer. The present invention is directed to compns. comprising at least one immunoconjugate and at least one chemotherapeutic agent and to methods of treating cancer using at least one immunoconjugate and at least one chemotherapeutic agent. The present invention also provides methods of modulating the growth of selected cell populations. such as cancer cells. by administering a therapeutically effective amount of at least one chemotherapeutic agent and at least one immunoconjugate.

IT **186692-73-9**. Epothilone C **189453-10-9**. Epothilone D
RL: BAC (Biological activity or effector. except adverse): BSU (Biological study. unclassified): THU (Therapeutic use): BIOL (Biological study): USES

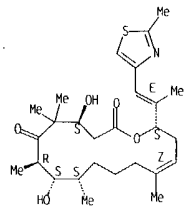
L5 ANSWER 40 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(Uses)
(chemotherapeutic agent; compns. and methods for treating cancer and other diseases using immunoconjugates and chemotherapeutic agents)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13Z.16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9.13-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13Z.16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:195837 CAPLUS
DOCUMENT NUMBER: 134:222565
TITLE: Synthesis of epothilones. intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype
INVENTOR(S): Danishefsky. Samuel J.; Bertinato. Peter; Su. Dai-Shi; Meng. Dongfang; Chou. Ting-Chao; Kamenecka. Ted; Sorensen. Erik J.; Balog. Aaron; Savin. Kenneth A.; Kuduk. Scott; Harris. Christina; Zhang. Xiu-Guo; Bertino. Joseph R.
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research. USA
SOURCE: U.S.. 164 pp.. Cont.-in-part of Ser. No. US 1997-986025. filed on 3 Dec 1997
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6204388	B1	20010320	US 1999-257072	19990224 <--
US 6242469	B1	20010605	US 1997-986025	19971203 <--
EP 1386922	A2	20040204	EP 2003-22736	19971203
EP 1386922	A3	20040407		
R: BE. CH. DE. FR. GB. IT. LI. NL. SE				
ZA 9901497	A	19990824	ZA 1999-1497	19990224 <--
US 6316630	B1	20011113	US 2000-588925	20000606 <--
US 6300355	B1	20011009	US 2000-662426	20000913 <--
US 6369234	B1	20020409	US 2000-686158	20001011
US 6284781	B1	20010904	US 2000-691615	20001018 <--
US 2002058286	A1	20020516	US 2001-797027	20010301
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US 2002002194	A1	20020103	US 2001-874514	20010605
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US 2003069277	A1	20030410	US 2002-135433	20020430
US 2003208080	A1	20031106	US 2002-329090	20021223
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PRIORITY APPLN. INFO.: US 1996-32282P P 19961203
US 1997-33767P P 19970114
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US 1997-55533P P 19970813
US 1997-986025 A2 19971203
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L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 1998-92319P	P	19980709
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EP 1997-954055	A3	19971203
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US 2001-874514	A1	20010605
US 2001-4571	A1	20011204
US 2002-58695	A1	20020128
US 2002-62376	A1	20020201
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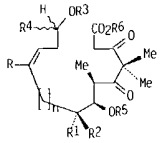
US 2003-374805	A1	20030225

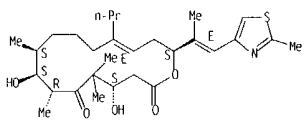
OTHER SOURCE(S): MARPAT 134:222565
GRAPHIC IMAGE:



I

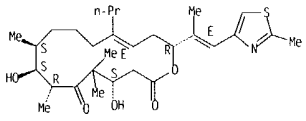
ABSTRACT:
Syntheses of epothilone A and B, desoxyepothilones A and B, and protected ketoester precursors (I) [R,R1,R2 = independently H, (un)substituted linear or branched chain alkyl; R3 = CHY=CHX, H, linear or branched chain alkyl, Ph, 2-methyl-1,3-thiazolinyl, 2-, 3-, or 4-furanyl, 2-, 3-, or 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3- or 6-indolyl; X = H, linear or branched chain alkyl, Ph, 2-methyl-1,3-thiazolinyl, 2-, 3-, or 4-furanyl, 2-, 3-, or 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3- or 6-indolyl; Y = H, linear or branched chain alkyl;X = O, substituted NOH, substituted NNH2; n = 1-2, R4 = linear or branched chain alkyl, (un)substituted aryloxyalkyl, trialkylsilyl, aryldialkylsilyl, diarylalkylsilyl, troarylsilyl; R5 = tertiaryalkyl; R6 = H, t-butyloxycarbonyl, amyloxycarbonyl, (trialkylsilyl)alkyloxycarbonyl, (dialkylarylsilyl)alkoxycarbonyl, benzyl, trialkylsilyl, dialkylarylsilyl, alkylarylsilyl,triarylsilyl, linear or branched acyl, (un)substituted aroyl] and their intermediates are described. Activities of novel compns. based on epothilones and I and methods for the treatment of cancer and cancer which has developed a multidrug-resistant phenotype are presented.

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 219824-14-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



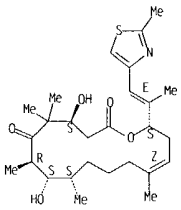
IT **198475-04-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)
RN 198475-04-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **189453-10-9P**, Desoxyepothilone B **198475-05-7P**
219824-14-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

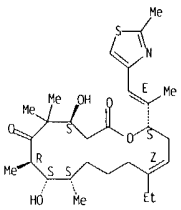
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198475-05-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

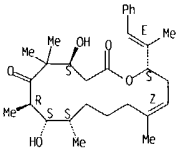
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **198475-13-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)
RN 198475-13-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

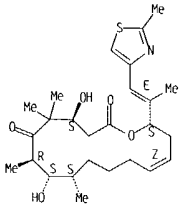
Absolute stereochemistry.
Double bond geometry as shown.



IT **186692-73-9**, Desoxyepothilone A **188259-95-2**
188260-10-8 **189453-40-5** **192370-82-4**
198475-06-8 **198475-07-9** **198475-11-5**
198475-12-6 **219824-38-1** **241129-05-5**
241129-07-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)
RN 186692-73-9 CAPLUS

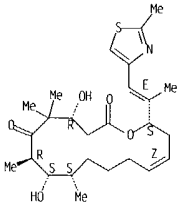
L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188259-95-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

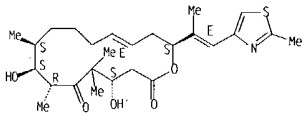
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-

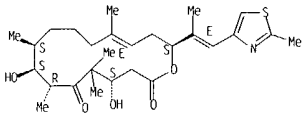
L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

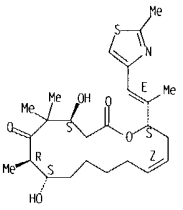
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 192370-82-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

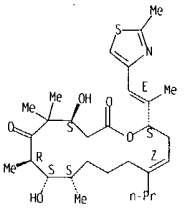
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-06-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

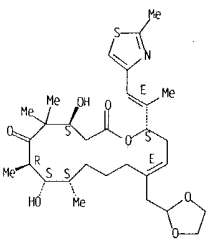
Absolute stereochemistry.
Double bond geometry as shown.



RN 198475-07-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(1,3-dioxolan-2-ylmethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

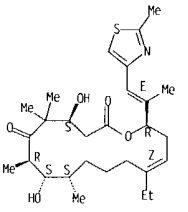
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-11-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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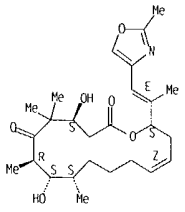
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

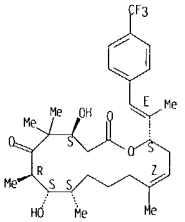
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 219824-38-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-[4-(trifluoromethyl)phenyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

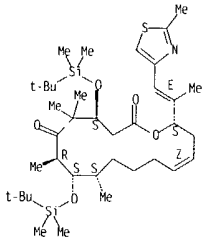
Absolute stereochemistry.
Double bond geometry as shown.



RN 241129-05-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-pentyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

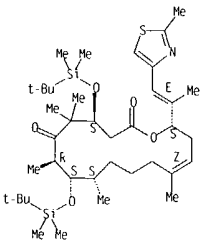
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 241129-07-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-pentyl-.

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

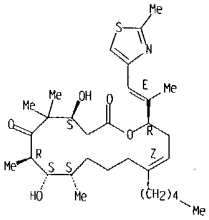


RN 209261-05-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-ethyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(4S,7R,8S,9S,13Z,16R)- (9CI) (CA INDEX NAME)

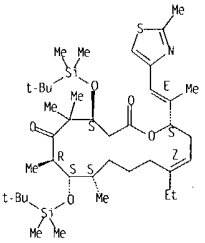
Absolute stereochemistry.
Double bond geometry as shown.



IT **186692-84-2P 189453-35-8P 209261-05-2P**
219824-09-6P 219824-13-2P 219824-19-8P
219824-25-6P 219824-29-0P 241129-40-8P
241129-41-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)
RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

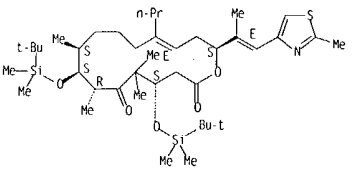
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 219824-09-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

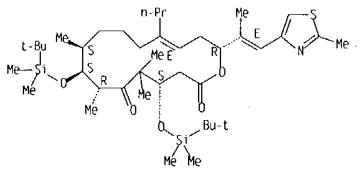
Absolute stereochemistry.
Double bond geometry as shown.



RN 219824-13-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16R)- (9CI) (CA INDEX NAME)

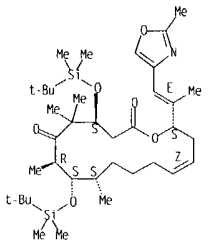
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 219824-19-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

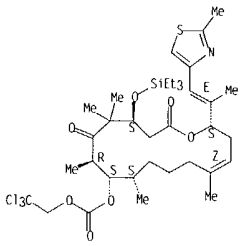
Absolute stereochemistry.
Double bond geometry as shown.



RN 219824-25-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

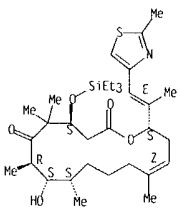
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



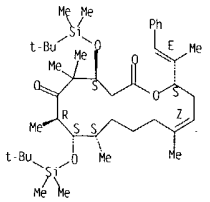
RN 241129-41-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



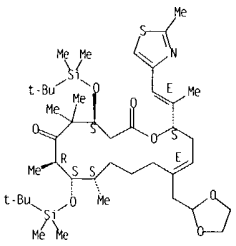
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 41 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 219824-29-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(1,3-dioxolan-2-ylmethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 241129-40-8 CAPLUS
CN Carbonic acid, (4S,7R,8S,9S,13Z,16S)-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-2,6-dioxo-4-[(triethylsilyl)oxy]oxacyclohexadec-13-en-8-yl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

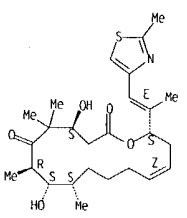
Absolute stereochemistry. Rotation (-).

L5 ANSWER 42 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:158443 CAPLUS
DOCUMENT NUMBER: 134:325271
TITLE: Studies on the biosynthesis of epothilones: the PKS and epothilone C/D monooxygenase
AUTHOR(S): Gerth, Klaus; Steinmetz, Heinrich; Höfle, Gerhard; Reichenbach, Hans
CORPORATE SOURCE: GBF, Gesellschaft fur Biotechnologische Forschung mbH, Abteilung Naturstoffbiologie, Braunschweig, D-38124, Germany
SOURCE: Journal of Antibiotics (2001), 54(2), 144-148
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Nonproducer mutants support the assumption that epothilones A and B are synthesized by the same polyketide synthase (PKS). The endproducts of the PKS, epothilones C and D, compete for the active site of a constitutively synthesized monooxygenase which is regulated by product inhibition. The postulated C-13 hydroxy-epothilones as direct precursors of epothilones C and D were not detected.

IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(polyketide synthase and epothilone C/D monooxygenase in epothilone biosynthesis)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

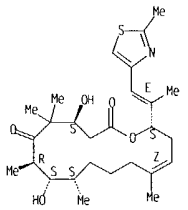
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 42 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

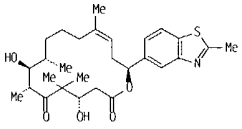
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 43 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:138738 CAPLUS
DOCUMENT NUMBER: 134:311010
TITLE: Synthetic epothilone analogs with modifications in the northern hemisphere and the heterocyclic side-chain-synthesis and biological evaluation
AUTHOR(S): End, Nicole; Bold, Guido; Caravatti, Giorgio; Wartmann, Markus; Altmann, Karl-Heinz
CORPORATE SOURCE: TA Oncology Research, Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Proceedings of ECSOC-3, [and] Proceedings of ECSOC-4, Sept. 1-30, 1999 and 2000 (2000), Meeting Date 1999-2000, 1431-1442. Editor(s): Pombo-Villar, Esteban. Molecular Diversity Preservation International: Basel, Switz.
CODEN: 69AXZT
DOCUMENT TYPE: Conference; (computer optical disk)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:311010
GRAPHIC IMAGE:



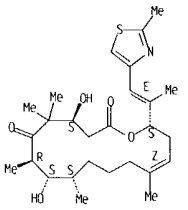
I

ABSTRACT:
The authors have synthesized epothilone analogs, e.g. I, with modifications in the northern hemisphere and the heterocyclic side-chain. In all three cases the key steps for construction of the macrocyclic skeleton involve Yamaguchi macrolactonization, the build-up of the requisite seco-acid through aldol reaction between the C7-C15 aldehyde and the dianion of the O-protected C1-C6 β-hydroxy acid fragment, and the assembly of the C7-C15 aldehyde through the appropriate type of Pd(0)-catalyzed coupling reaction. The IC50 for growth inhibition of the KB-31 tumor cell line for I was 0.45 nM.

IT **189453-10-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

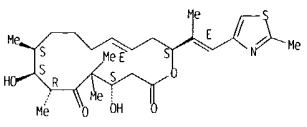
L5 ANSWER 43 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(synthetic epothilone analogs with modifications in the northern hemisphere and the heterocyclic side-chain-synthesis and biol. evaluation)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **188260-10-8P 188260-22-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthetic epothilone analogs with modifications in the northern hemisphere and the heterocyclic side-chain-synthesis and biol. evaluation)
RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

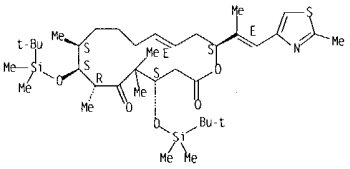
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-22-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-

L5 ANSWER 43 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

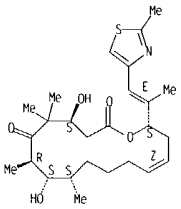


REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:137877 CAPLUS
DOCUMENT NUMBER: 134:335980
TITLE: Comparative molecular field analysis (CoMFA) study of epothilones - tubulin depolymerization inhibitors: pharmacophore development using 3D QSAR methods
AUTHOR(S): Lee, Keun Woo; Briggs, James M.
CORPORATE SOURCE: Department of Biology and Biochemistry, University of Houston, Houston, TX, 77204-5513, USA
SOURCE: Journal of Computer-Aided Molecular Design (2001), 15(1), 41-55
CODEN: JCADEQ; ISSN: 0920-654X
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A three-dimensional quant. structure-activity relationship (3D QSAR) study has been carried out on epothilones based on comparative mol. field analyses (CoMFA) using a large data set of epothilone analogs, which are potent inhibitors of tubulin depolymn. Microtubules, which are polymers of the α/β-tubulin heterodimer, need to dissociate in order to form the mitotic spindle, a structure required for cell division. A rational pharmacophore searching method using 3D QSAR procedures was carried out and the results for the epothilones are described herein. One-hundred and sixty-six epothilone analogs and their depolymn. inhibition properties with tubulin were used as a training set. Over a thousand mol. field energies were generated and applied to generate the descriptors of QSAR equations. Using a genetic function algorithm (GFA) method, combined with a least square approach, multiple QSAR models were considered during the search for pharmacophore elements. Each GFA run resulted in 100 QSAR models, which were ranked according to their lack of fit (LOF) scores, with a total of 40 GFA runs having been performed. The 40 best QSAR equations from each run had adequate fitted correlation coeffs. (R from 0.813 to 0.863) and were of sufficient statistical significance (F value from 7.2 to 10.9). The pharmacophore elements for epothilones were studied by investigating the hit frequency of descriptors (i.e. the sampling probabilities of grid points from the GFA studies) from the set of the 4000 top scoring QSAR equations. By comparing the frequency with which each grid point appeared in the QSAR equations, three candidate regions in the epothilones were proposed to be pharmacophore elements. Two of them are completely compatible with the recent model proposed by Ojima et al. however, one is quite different and is necessary to accurately predict the activities of all 166 epothilone mols. used in our training set. Finally, by visualizing the 35 most probable grid points, it was found that changes related to the C6, C7, C8, C12, S20, and C21 atoms of the epothilones were highly correlated to their activity.

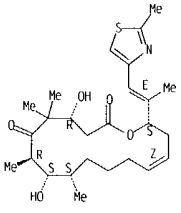
IT **186692-73-9 188259-95-2 188260-10-8**
188260-34-6 189453-10-9 189453-40-5

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 188259-95-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



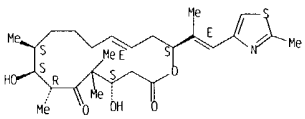
RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
192370-82-4 193071-86-2 193146-35-9
198475-04-6 198475-12-6 198571-09-4
198571-10-7 198571-11-8 198571-15-2
198571-16-3 198571-17-4 198571-18-5
198571-19-6 198571-20-9 198571-21-0
198571-22-1 198571-24-3 198571-25-4
198571-26-5 198571-28-7 198571-29-8
198571-30-1 198571-31-2 198571-32-3
198571-33-4 198571-66-3 198571-67-4
198571-68-5 198571-69-6 198571-70-9
198571-71-0 198571-72-1 198571-73-2
198571-74-3 198571-76-5 198571-77-6
198571-78-7 201136-85-8 201136-86-9
201136-88-1 201136-91-6 201136-92-7
204513-12-2 204513-16-6 204513-30-4
204513-35-9 204513-36-0 204513-39-3
204513-40-6 204513-41-7 204513-42-8
204513-43-9 204513-44-0 204513-45-1
204513-46-2 204513-47-3 204513-50-8
204513-51-9 204513-52-0 204513-53-1
209260-91-3 240816-37-9 240816-39-1
252981-42-3 337981-53-0 337981-57-4
337981-58-5 337981-59-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(CoMFA study of epothilones - tubulin depolymn. inhibitors: pharmacophore development using 3D QSAR methods)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

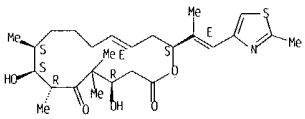
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



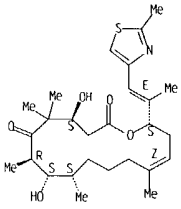
RN 188260-34-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

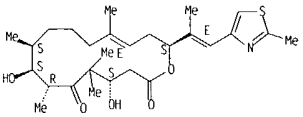
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-40-5 CAPLUS

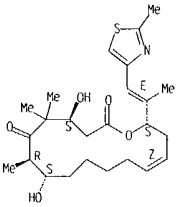
L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 192370-82-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

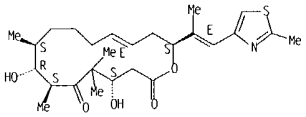
Absolute stereochemistry.
Double bond geometry as shown.



RN 193071-86-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

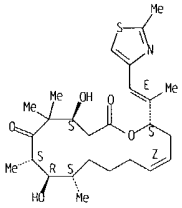
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 193146-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

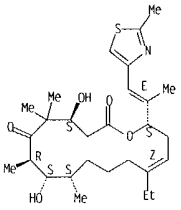
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198475-04-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

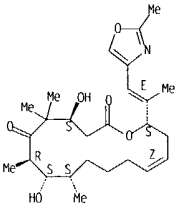
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

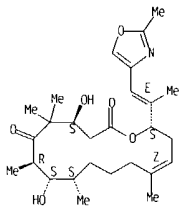
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-09-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

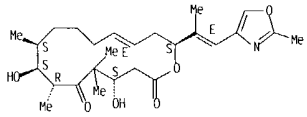
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



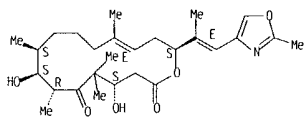
RN 198571-10-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-11-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

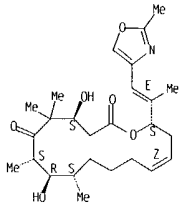
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-15-2 CAPLUS

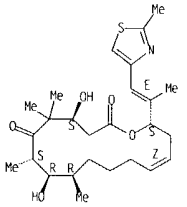
L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-16-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9R,13Z,16S)-(9CI) (CA INDEX NAME)

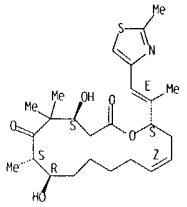
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-17-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,13Z,16S)- (9CI) (CA

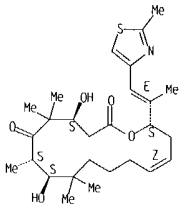
L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



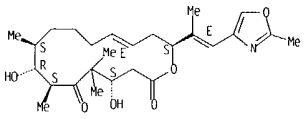
RN 198571-18-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



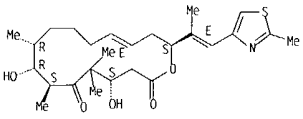
RN 198571-19-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



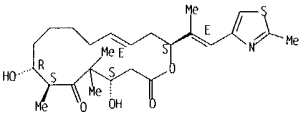
RN 198571-20-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



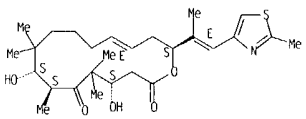
RN 198571-21-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



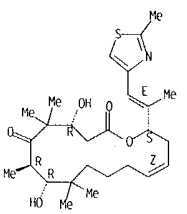
RN 198571-22-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8S,13E,16S)-(9CI) (CA INDEX NAME)

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.
Double bond geometry as shown.



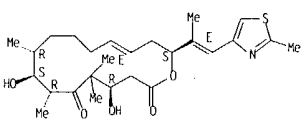
RN 198571-24-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8R,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-25-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9R,13E,16S)-(9CI) (CA INDEX NAME)

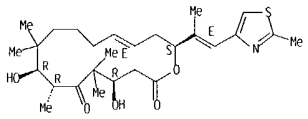
Absolute stereochemistry.
Double bond geometry as shown.



L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

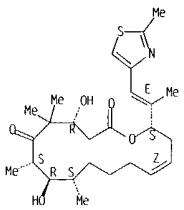
RN 198571-26-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-28-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

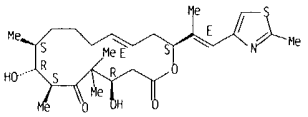
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-29-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9R,13Z,16S)-(9CI) (CA INDEX NAME)

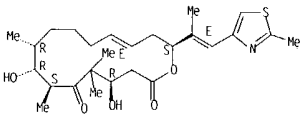
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



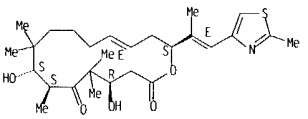
RN 198571-32-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-33-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8S,13E,16S)-(9CI) (CA INDEX NAME)

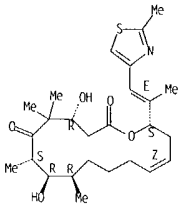
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-66-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13E,16S)-(9CI) (CA INDEX NAME)

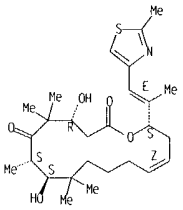
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-30-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8S,13Z,16S)-(9CI) (CA INDEX NAME)

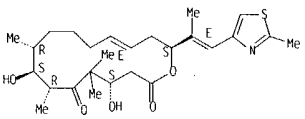
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-31-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

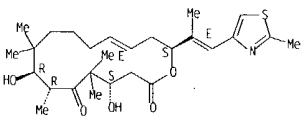
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



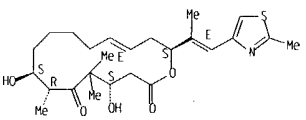
RN 198571-67-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-68-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13E,16S)- (9CI) (CA INDEX NAME)

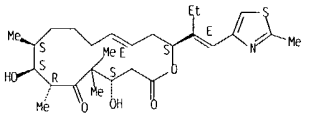
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-69-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-[(2-methyl-4-thiazolyl)methylene]propyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

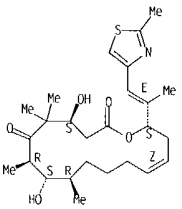
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-70-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13Z,16S)-(9CI) (CA INDEX NAME)

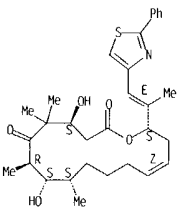
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-71-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8R,13Z,16S)-(9CI) (CA INDEX NAME)

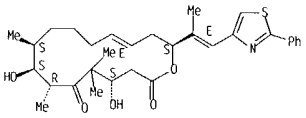
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



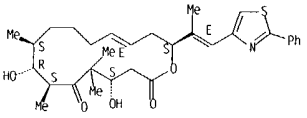
RN 198571-74-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



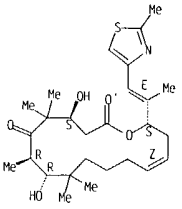
RN 198571-76-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



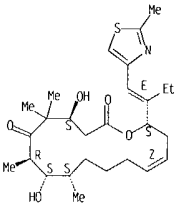
RN 198571-77-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-72-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-[(2-methyl-4-thiazolyl)methylene]propyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

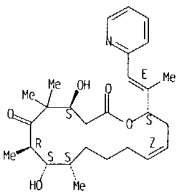


RN 198571-73-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

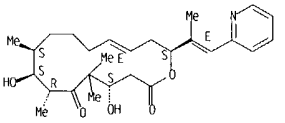
L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-78-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

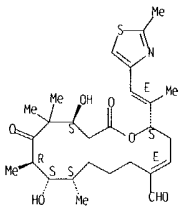
Absolute stereochemistry.
Double bond geometry as shown.



RN 201136-85-8 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxaldehyde, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

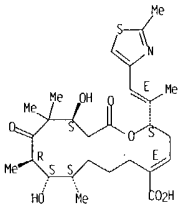
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-86-9 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxylic acid, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

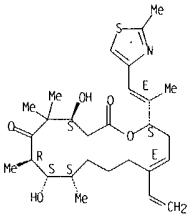
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-88-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(chloromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

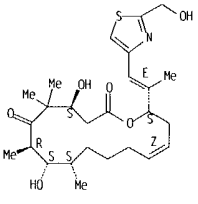
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-12-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

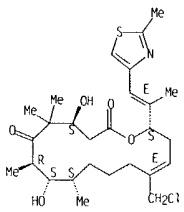
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 204513-16-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

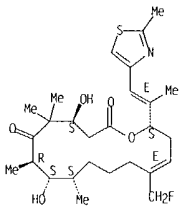
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-91-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(fluoromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

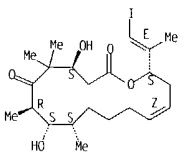
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-92-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethenyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

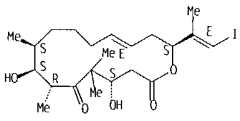
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



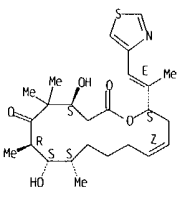
RN 204513-30-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

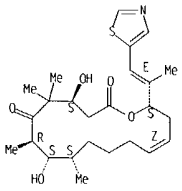
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-36-0 CAPLUS

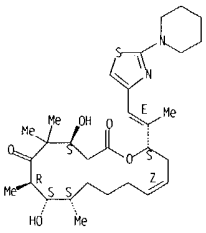
L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



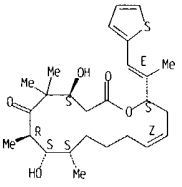
RN 204513-39-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(1-piperidinyl)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



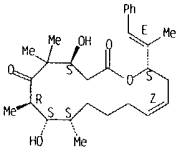
RN 204513-40-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-43-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-44-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 204513-41-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 204513-42-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 204513-45-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

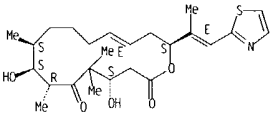
RN 204513-46-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

RN 204513-47-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-

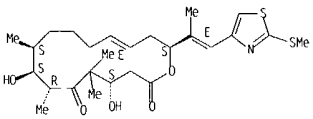
L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-thiazolyl)ethenyl]-. (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-50-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-. (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

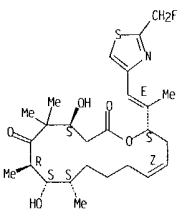


RN 204513-51-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

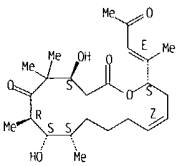
L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 240816-37-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-3-oxo-1-butenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

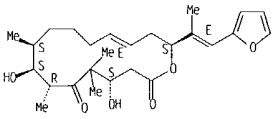
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-39-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-3-oxo-1-butenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

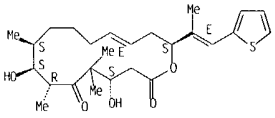
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



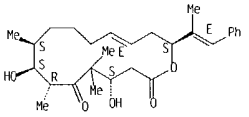
RN 204513-52-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



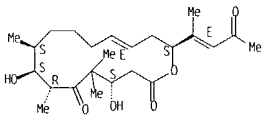
RN 204513-53-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



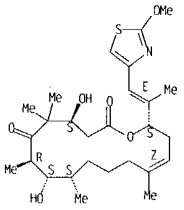
RN 209260-91-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 252981-42-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-(2-methoxy-4-thiazolyl)-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

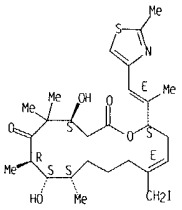
Absolute stereochemistry.
Double bond geometry as shown.



RN 337981-53-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(iodomethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

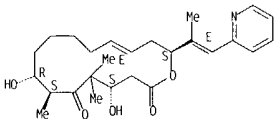
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 337981-57-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7S,8R,13E,16S)- (9CI) (CA INDEX NAME)

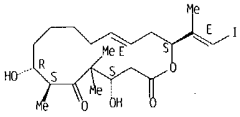
Absolute stereochemistry.
Double bond geometry as shown.



RN 337981-58-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7-trimethyl-, (4S,7S,8R,13E,16S)- (9CI) (CA INDEX NAME)

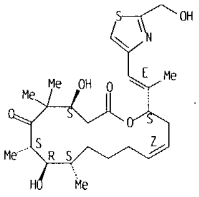
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 44 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 337981-59-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7S,8R,9S,13Z,16S)- (9CI) (CA INDEX NAME)

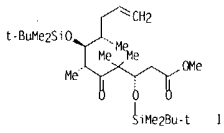
Absolute stereochemistry.
Double bond geometry as shown.



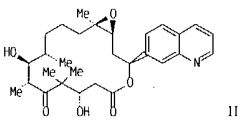
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 45 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:853645 CAPLUS
DOCUMENT NUMBER: 134:178371
TITLE: Synthesis and biological evaluation of highly potent analogues of epothilones B and D
AUTHOR(S): Altmann, K.-H.; Bold, G.; Caravatti, G.; Florsheimer, A.; Guagnano, V.; Wartmann, M.
CORPORATE SOURCE: Novartis Pharma AG, TA Oncology Research, Basel, CH-4002, Switz.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(24), 2765-2768
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:178371
GRAPHIC IMAGE:



I



II

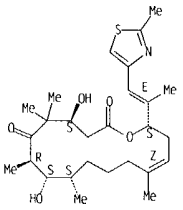
ABSTRACT:
A series of new epothilone B and D analogs incorporating fused hetero-aromatic side chains have been prepared. The synthetic strategy is based on olefin I as the common intermediate and allows variation of the side-chain structure in a highly convergent and stereoselective manner. These epothilone analogs, e.g. II, are more potent inhibitors of cancer cell proliferation than the corresponding parent epothilones B or D.

IT **189453-10-9**, Epothilone D
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and biol. evaluation of highly potent analogs of epothilones

L5 ANSWER 45 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
B and D)

RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



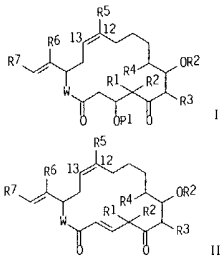
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 46 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:842116 CAPLUS
DOCUMENT NUMBER: 133:362657
TITLE: A process for the reduction of oxiranyl epothilones to olefinic epothilones
INVENTOR(S): Kim, Soong-Hoon; Johnson, James A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000071521	A1	20001130	WO 2000-US13253	20000515 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6320045	B1	20011120	US 1999-316796	19990521 <--
EP 1178968	A1	20020213	EP 2000-930725	20000515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500394	T2	20030107	JP 2000-619778	20000515

PRIORITY APPLN. INFO.: US 1999-316796 A 19990521
US 1997-67549P P 19971204
US 1998-82563P P 19980421
US 1998-170581 A2 19981013
WO 2000-US13253 W 20000515
OTHER SOURCE(S): CASREACT 133:362657; MARPAT 133:362657
GRAPHIC IMAGE:

L5 ANSWER 46 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

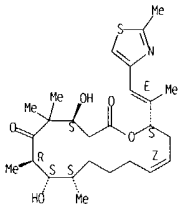
II

ABSTRACT:
12(13)-Olefinic epothilones, such as I and II [R1-6 = H, alkyl, aryl; R1R2 = cycloalkyl; R7 = H, alkyl, aryl, cycloalkyl, heterocyclyl; P1, P2 = H, alkyl, alkanoyl, aroyl, silyl, etc.; W = O, NR8; R8 = H, OH, alkyl], were prepared via reduction of the corresponding 12,13-epoxyepothilones using a metal or metal-assisted reagent. The metal or metal-assisted reagent was selected from the group consisting of reactive metallocenes, [N2C(CO2Me)2, cat Rh2(OAc)4], [N2C(CO2Me)2, cat[(n-C7H15CO2)2Rh]2], [Zn-Cu, EtOH], [Mg(Hg), MgBr], Cr, [FeCl3, n-BuLi], [TiCl3, LiAlH4], [TiCl4, Zn], [WCl6, LiAlH4], [NbCl5, NaAlH4], [VCl3,Zn], or [WCl6, n-BuLi]. Thus, epothilone A, a 12,13-epoxyepothilone, was reduced using magnesium turnings and titanocene dichloride in THF to give epothilone C, a 12(13)-(Z)-olefin, in 80% yield.

IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
226956-19-0P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the reduction of oxiranyl epothilones to olefinic epothilones)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

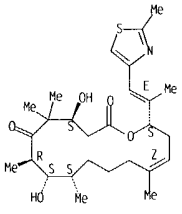
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 46 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

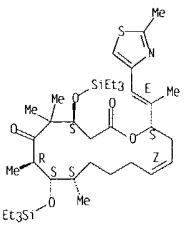
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 226956-19-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 46 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



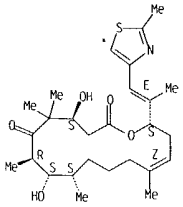
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 47 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:739098 CAPLUS
DOCUMENT NUMBER: 134:56491
TITLE: Epothilones: microtubule stabilizing agents with enhanced activity against multidrug-resistant cell lines and tumors
AUTHOR(S): Harris, Christina R.; Balog, Aaron; Savin, Kenneth; Danishefsky, Samuel J.; Chou, Ting Chao; Zhang, Xiu-Guo
CORPORATE SOURCE: The Laboratory for Bioorganic Chemistry, New York, NY, 10021, USA
SOURCE: Actualites de Chimie Therapeutique (1999), 25, 187-206
CODEN: ACHTD9; ISSN: 0338-8999
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with 33 refs. on the synthesis and biol. activity of epothilones. Highly efficient, highly convergent total syntheses involving ring-closing olefin metathesis, Suzuki coupling, stereoselective aldol reactions and stereoselective Noyori redns. are discussed.

IT **189453-10-9P**, Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilones as microtubule stabilizing agents with enhanced activity against multidrug-resistant cell lines and tumors)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

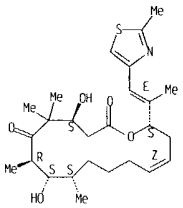
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 47 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **186692-73-9**, Desoxyepothilone A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of epothilones as microtubule stabilizing agents with enhanced activity against multidrug-resistant cell lines and tumors)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



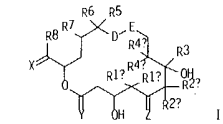
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 47 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L5 ANSWER 48 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:738730 CAPLUS
DOCUMENT NUMBER: 133:309795
TITLE: Preparation of new epothilone derivatives and their pharmaceutical uses
INVENTOR(S): Klar, Ulrich; Schwede, Wolfgang; Skuballa, Werner; Buchmann, Bernd; Schirner, Michael
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 74 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19908767	A1	20001019	DE 1999-19908767	19990218 <--

PRIORITY APPLN. INFO.: DE 1999-19908767 19990218
OTHER SOURCE(S): MARPAT 133:309795
GRAPHIC IMAGE:



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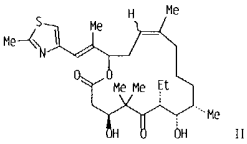


II

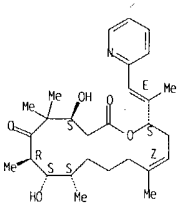
ABSTRACT:
New epothilone derivs. I (R1a,R1b = R2a,R2b = same or different H, alkyl, aryl, aralkyl or (CH2)m,n m, n = 2-5; R3 = H, alkyl, aryl, aralkyl; R4a,R4b = same or different H, alkyl, aryl, aralkyl or (CH2)p = 2-5, CH2CH2, CH=CH, C.tplbond.C, epoxy, CH(OH)CH(OH), CH(OH)CH2; D-E = a group; R5 = H, alkyl, aryl, aralkyl; R6,R7 = H, bond, O; R8 = H, alkyl, aryl, aralkyl; X = O, OR23 alkylene-α,-ω-dioxy group straight or branched, OR9 or the CR10R11

L5 ANSWER 48 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
group where R23 = alkyl, R9 = H or protecting group and R10,R11 = same or different H, alkyl, aryl, aralkyl or R10,R11 = together with methylene are a 5-7 membered carbocyclic ring; Y = O or two H; Z = O or H/OR12 and R12 = H or a protecting group) were prepd. Thus E- and Z-II were prepd. via a multistep synthesis. I cooperate with tubulin by stabilizing formed microtubuli. I are able phase specifically to affect the cell division and are suitable for the treatment of malignant ovarian, stomach, colon, adeno, breast, lung, head and neck tumors, malignant melanomas, acute lymphocytic and myelocytic leukemia. Derivs. of I are suitable for use in anti-angiogenic therapy as well as for treating chronic inflammatory diseases (psoriasis, arthritis). In order to prevent uncontrolled cell proliferations and to improve the compatibility of medical implants I can be applied or incorporated into polymeric materials. I can be used alone or to achieve additive or synergistic effects in combination with further principles and substance classes applicable in tumor therapy.

IT **220773-73-9P 220773-76-2P 220773-79-5P**
301856-94-0P 301856-95-1P 301856-98-4P
301856-99-5P 301857-08-9P 301857-14-7P
301857-17-0P 301857-23-8P 301857-26-1P
301857-29-4P 301857-36-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of new epothilone derivs. and their pharmaceutical uses)

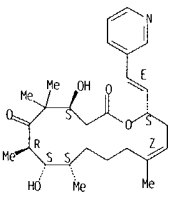
RN 220773-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



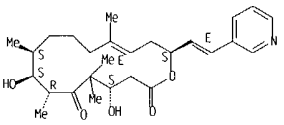
RN 220773-76-2 CAPLUS

L5 ANSWER 48 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 301856-95-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

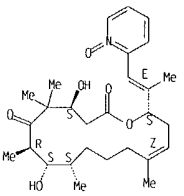


RN 301856-98-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-2-(4-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

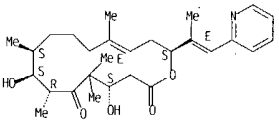
L5 ANSWER 48 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(1-oxido-2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 220773-79-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

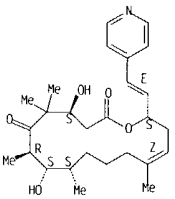
Absolute stereochemistry.
Double bond geometry as shown.



RN 301856-94-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

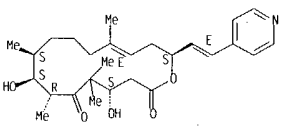
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 48 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



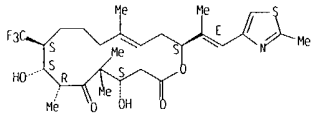
RN 301856-99-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-2-(4-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 301857-08-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,13-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-9-(trifluoromethyl)-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

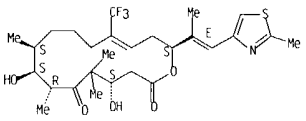
Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 301857-14-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-

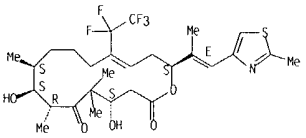
L5 ANSWER 48 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-(trifluoromethyl)-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 301857-17-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-(pentafluoroethyl)-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

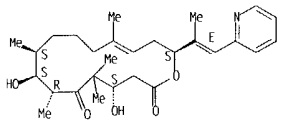
Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 301857-23-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

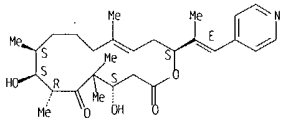
Absolute stereochemistry.
Double bond geometry as described by E or Z.

L5 ANSWER 48 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



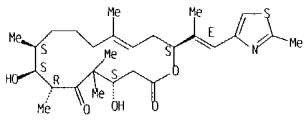
RN 301857-26-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(4-pyridinyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 301857-29-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

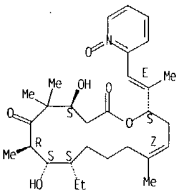
Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 301857-36-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 9-ethyl-4,8-dihydroxy-5,5,7,13-tetramethyl-16-[(1E)-1-methyl-2-(1-oxido-2-pyridinyl)ethenyl]-.

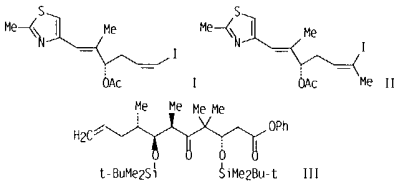
L5 ANSWER 48 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L5 ANSWER 49 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:733774 CAPLUS
DOCUMENT NUMBER: 134:56502
TITLE: Enantioselective Total Synthesis of Epothilones A and B Using Multifunctional Asymmetric Catalysis
AUTHOR(S): Sawada, Daisuke; Kanai, Motomu; Shibasaki, Masakatsu
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, The University of Tokyo, Bunkyo-ku Tokyo, 113-0033, Japan
SOURCE: Journal of the American Chemical Society (2000), 122(43), 10521-10532
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:56502
GRAPHIC IMAGE:

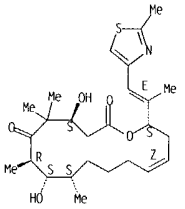


ABSTRACT:
An enantioselective total synthesis of epothilones A and B using multifunctional asym. catalysis such as a cyanosilylation of an aldehyde, an aldol reaction of an unmodified ketone with an aldehyde, and a protonation in the conjugate addition of a thiol to an α,β-unsatd. thioester has been achieved. Epothilones A and B were divided into fragment A (I), fragment B (II), and fragment C (III). A catalytic asym. synthesis of fragments A and B was accomplished using a catalytic asym. cyanosilylation as a key step. An enantiocontrolled synthesis of fragment C was achieved in two ways. One is the use of a direct catalytic asym. aldol reaction of an unmodified ketone with an aldehyde as a key step, and the other utilizes a catalytic asym. protonation in the conjugate addition of a thiol to an α,β-unsatd. thioester as a key step. Suzuki cross-coupling of fragment A with fragment C followed by Yamaguchi lactonization as key steps led to an enantiocontrolled synthesis of epothilone A. On the other hand, Suzuki cross-coupling of fragment B with fragment C followed by Yamaguchi lactonization accomplished an enantiocontrolled synthesis of epothilone B.

IT 186692-73-9P, Epothilone C 186692-84-2P
189453-10-9P, Epothilone D 189453-35-8P

L5 ANSWER 49 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enantioselective total synthesis of epothilones A and B using multifunctional asym. catalysis)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

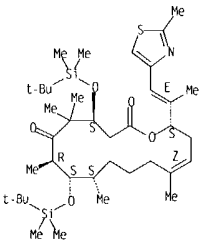
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

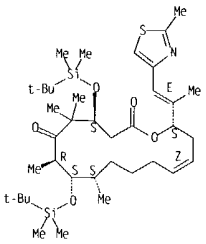
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 49 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



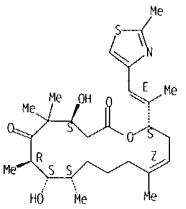
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 49 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

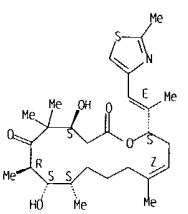
L5 ANSWER 50 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2000:701228 CAPLUS
DOCUMENT NUMBER:	134:4795
TITLE:	Total Syntheses of Epothilones B and D
AUTHOR(S):	Mulzer, Johann; Mantoulidis, Andreas; Oehler, Elisabeth
CORPORATE SOURCE:	Institut fuer Organische Chemie, Universitaet Wien, Vienna, A-1090, Austria
SOURCE:	Journal of Organic Chemistry (2000), 65(22), 7456-7467 CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 134:4795

ABSTRACT:
Total syntheses of the microtubule stabilizing antitumor drugs epothilone B and D are described, starting from optically pure (S)-malic acid and Me (R)-3-hydroxy-2-methylpropionate. The synthesis is highly convergent by coupling the three fragments C1-C6 (fragment D), C7-C10 (fragment C), and C11-C21 (fragment B). Key steps are two stereoselective Wittig type olefinations to generate the 12,13- and 16,17-double bonds, an enantioselective Mukaiyama aldol addition to synthesize fragment D, and a sulfone anion allyl iodide alkylation to connect fragments B and C. Finally fragment D was attached to the B + C fragment via aldol addition

IT **189453-10-9P**, Epothilone D **189453-35-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total syntheses of epothilones B and D)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

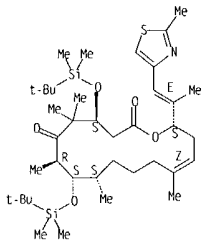
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 50 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

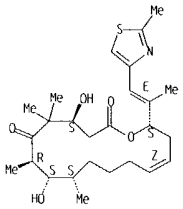


REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 51 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:656305 CAPLUS
DOCUMENT NUMBER: 134:85141
TITLE: Epothilone from amphora
AUTHOR(S): Jaenicke, Lothar
CORPORATE SOURCE: Universitat Koeln, Cologne, Germany
SOURCE: Chemie in Unserer Zeit (2000), 34(4), 257
CODEN: CUNZAW; ISSN: 0009-2851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German
ABSTRACT:
A review with 3 refs. Epothilone synthesis in Sorangium cellulosum, the mode of action of epithilones, the gene-tech. production of epothilone in Streptomyces coelicolor CH999, and possible manipulations in the polyketide synthetase module are reviewed.

IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: BMF (Bioindustrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fermentative production of epothilone by Streptomyces coelicolor)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

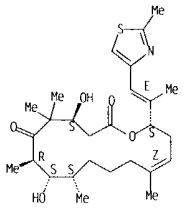
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

L5 ANSWER 51 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



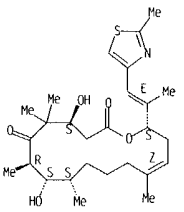
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 52 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:624043 CAPLUS
DOCUMENT NUMBER: 133:266634
TITLE: Total Synthesis and Antitumor Activity of 12,13-Desoxyepothilone F: An Unexpected Solvolysis Problem at C15, Mediated by Remote Substitution at C21
AUTHOR(S): Lee, Chul Bom; Chou, Ting-Chao; Zhang, Xiu-Guo; Wang, Zhi-Guang; Kuduk, Scott D.; Chappell, Mark D.; Stachel, Shawn J.; Danishefsky, Samuel J.
CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, The Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Journal of Organic Chemistry (2000), 65(20), 6525-6533
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:266634
ABSTRACT:
A new epothilone analog, 12,13-desoxyepothilone F (dEpoF, 21-hydroxy-12,13-desoxyepothilone B, 21-hydroxyepothilone D), was synthesized and evaluated for antitumor potential. A convergent strategy employed for the semi-practical synthesis of 12,13-desoxyepothilone B (dEpoB) has been utilized to yield an amount of dEpoF sufficient for relevant biol. studies. The results from an in vitro assay reveal that this new analog is highly active against various tumor cell lines with a potency comparable to that of dEpoB. In particular, the growth of resistant tumor cells is inhibited by dEpoF at concns. where paclitaxel (Taxol) is basically ineffective. A preliminary assessment of its in vivo activity is also promising. The new analog, containing an addnl. hydroxyl group at C21, exhibits advantages over other epothilones in terms of water solubility, and can serve as a readily functionalizable handle to produce other useful compds. for pertinent biol. studies.

IT **189453-10-9**, 12,13-Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(aqueous solubility; total synthesis and antitumor activity of desoxyepothilone F)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

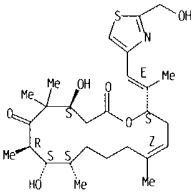
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 52 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



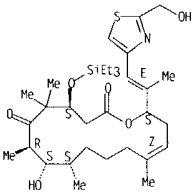
IT **252981-50-3P**, 12,13-Desoxyepothilone F
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(aqueous solubility; total synthesis and antitumor activity of desoxyepothilone F)
RN 252981-50-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **298702-21-3P 298702-22-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

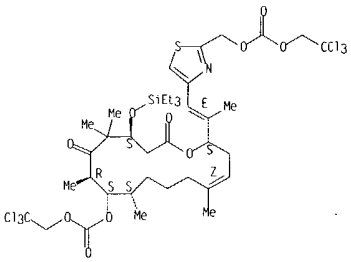
L5 ANSWER 52 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 52 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(total synthesis and antitumor activity of desoxyepothilone F)
RN 298702-21-3 CAPLUS
CN Carbonic acid, [4-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-5,9,11,13,13-pentamethyl-12,16-dioxo-10-[[(2,2,2-trichloroethoxy)carbonyl]oxy]-14-[(triethylsilyl)oxy]oxacyclohexadec-4-en-2-yl]-1-propenyl]-2-thiazolyl]methyl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 298702-22-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-4-[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 53 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

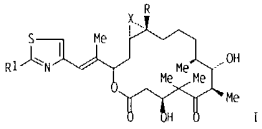
ACCESSION NUMBER: 2000:608747 CAPLUS
DOCUMENT NUMBER: 133:193030
TITLE: Preparation of C-21 modified epothilones for use as anticancer agents
INVENTOR(S): Hoefle, Gerhard; Glaser, Nicole; Leibold, Thomas; Vite, Gregory; Kim, Soong-Hoon
PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung Mbh (Gbf), Germany; Bristol-Myers Squibb Co.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050423	A1	20000831	WO 2000-US4068	20000217 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19907588	A1	20000824	DE 1999-19907588	19990222 <--
DE 19930111	A1	20010104	DE 1999-19930111	19990701 <--
CA 2360452	AA	20000831	CA 2000-2360452	20000217 <--
EP 1157023	A1	20011128	EP 2000-910219	20000217 <--
EP 1157023	B1	20031119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008379	A	20020924	BR 2000-8379	20000217
JP 2002537395	T2	20021105	JP 2000-601003	20000217
EE 200100437	A	20021216	EE 2001-437	20000217
AT 254615	E	20031215	AT 2000-910219	20000217
NO 2001004017	A	20011017	NO 2001-4017	20010817 <--
BG 105830	A	20020329	BG 2001-105830	20010817
LV 12755	B	20020420	LV 2001-126	20010823

PRIORITY APPLN. INFO.: DE 1999-19907588 A 19990222
DE 1999-19930111 A 19990701
WO 2000-US4068 W 20000217

OTHER SOURCE(S): MARPAT 133:193030
GRAPHIC IMAGE:

L5 ANSWER 53 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



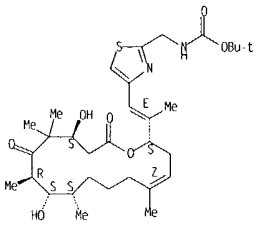
I

ABSTRACT:
C-21 modified epothilones, such as I [R = H, Me; R1 = H, alkyl, substituted alkyl, etc.; X = O, bond], were prepared for pharmaceutical uses, such as anticancer and antifungal agents. Thus, epothilone A N-oxide was reacted with valeric acid anhydride to give epothilone E 21-valerate in 40% yield. The prepared epothilones were tested for cytostatic activity against a variety of cancer cell lines, such as human cervix carcinoma KB-3.1 and PC-3 human prostate adenocarcinoma.

IT **289494-43-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of C-21 modified epothilones for use as anticancer agents)
RN 289494-43-5 CAPLUS
CN Carbamic acid, [[4-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-10,14-dihydroxy-5,9,11,13,13-pentamethyl-12,16-dioxooxacyclohexadec-4-en-2-yl]-1-propenyl]-2-thiazolyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

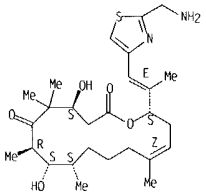
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 53 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **289494-44-6P 289494-61-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of C-21 modified epothilones for use as anticancer agents)
RN 289494-44-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(aminomethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

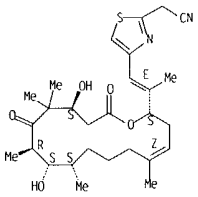
Absolute stereochemistry.
Double bond geometry as shown.



RN 289494-61-7 CAPLUS
CN 2-Thiazoleacetonitrile, 4-[(1E)-2-[(2S,4Z,9S,10S,11R,14S)-10,14-dihydroxy-5,9,11,13,13-pentamethyl-12,16-dioxooxacyclohexadec-4-en-2-yl]-1-propenyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 53 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

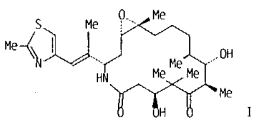
Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 54 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2000:597944 CAPLUS
DOCUMENT NUMBER:	133:321737
TITLE:	A Novel Application of a Pd(0)-Catalyzed Nucleophilic Substitution Reaction to the Regio- and Stereoselective Synthesis of Lactam Analogues of the Epothilone Natural Products
AUTHOR(S):	Borzilleri, Robert M.; Zheng, Xiaoping; Schmidt, Robert J.; Johnson, James A.; Kim, Soong-Hoon; DiMarco, John D.; Fairchild, Craig R.; Gougoutas, Jack Z.; Lee, Francis Y. F.; Long, Byron H.; Vite, Gregory D.
CORPORATE SOURCE:	Divisions of Discovery Chemistry Oncology Drug Discovery and Analytical Research and Development, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543-4000, USA
SOURCE:	Journal of the American Chemical Society (2000), 122(37), 8890-8897 CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 133:321737
GRAPHIC IMAGE:	



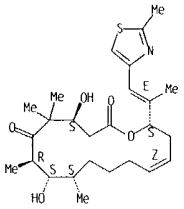
I

ABSTRACT:
Several lactam analogs of the epothilones were prepared using a concise semisynthetic approach starting with the unprotected natural products. Highlighted in this strategy is a novel regio- and stereoselective Pd(0)-catalyzed azidation reaction of a macrocyclic lactone. Subsequent reduction and macrolactamization of the resulting azide acid intermediates provided the desired macrolactams in satisfactory overall yields. The entire three-step sequence was streamlined into a "one-pot" process for the epothilone B-lactam, BMS-247550 (I), which is currently undergoing phase I clin. trials. An initial total synthesis route to prepare the lactam analog of epothilone C was completed and compared to the more direct semisynthesis approach. All of the lactam analogs were evaluated in vitro and the results are discussed.

IT **186692-73-9**, Epothilone C **189453-10-9**, Epothilone D

L5 ANSWER 54 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(application of a Pd(0)-catalyzed nucleophilic substitution reaction to the regio- and stereoselective synthesis of lactam analogs of the epothilone natural products)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

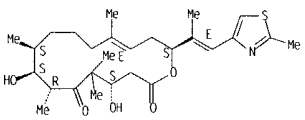
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

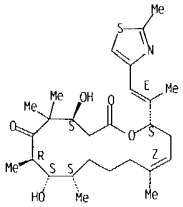
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 54 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



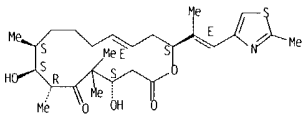
REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 54 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **188260-10-8 189453-40-5**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cytotoxicity; application of a Pd(0)-catalyzed nucleophilic substitution reaction to the regio- and stereoselective synthesis of lactam analogs of the epothilone natural products)
RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 55 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

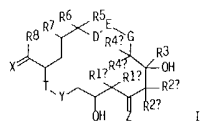
ACCESSION NUMBER:	2000:592721 CAPLUS
DOCUMENT NUMBER:	133:193028
TITLE:	Preparation of 16-halogen epothilone derivatives and their use as antitumor agents
INVENTOR(S):	Klar, Ulrich; Skuballa, Werner; Buchmann, Bernd; Schwede, Wolfgang; Schirner, Michael
PATENT ASSIGNEE(S):	Schering Aktiengesellschaft, Germany
SOURCE:	PCT Int. Appl., 105 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000049021	A2	20000824	WO 2000-EP1333	20000218 <--
WO 2000049021	A3	20001228		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19908765	A1	20000824	DE 1999-19908765	19990218 <--
DE 19954230	A1	20011115	DE 1999-19954230	19991104 <--
EP 1150980	A2	20011107	EP 2000-909205	20000218 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008331	A	20020129	BR 2000-8331	20000218
JP 2002537301	T2	20021105	JP 2000-599760	20000218
EE 200100431	A	20021216	EE 2001-431	20000218
BG 105802	A	20020329	BG 2001-105802	20010809
NO 2001004013	A	20011018	NO 2001-4013	20010817 <--
ZA 2001007648	A	20030107	ZA 2001-7648	20010917
US 6610736	B1	20030826	US 2001-913495	20011207
US 2004014978	A1	20040122	US 2003-364337	20030212

PRIORITY APPLN. INFO.:	DE 1999-19908765 A	19990218
	DE 1999-19954230 A	19991104
	WO 2000-EP1333 W	20000218
	US 2001-913495 A3	20011207
OTHER SOURCE(S):	MARPAT 133:193028	
GRAPHIC IMAGE:		

L5 ANSWER 55 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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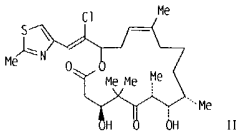


II

ABSTRACT:
16-Halogen epothilone derivs. I (R1a, R1b = R2a, R2b = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, (CH2)m m = 2-5; R3 = H, C1-C10-alkyl, aryl, C7-C20-aralkyl; G = O, CH2; R4a, R4b = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, (CH2)p p = 2-5; D-E = 1,2-ethanediyl, 1,2-ethenediyl, ethynyl, oxiranyl, 1,2-dihydroxy-1,2-ethanediyl, 1(2)-hydroxy-1,2-ethanediyl, CH2OH; R5 = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, CO2H, CO2-alkyl, CH2OH, CH2O-alkyl, CH2O-acyl, CN, CH2NH2, CH2N(alkyl, acyl)1,2, CH2-halogen; R6, R7 = H, bond, O; R8 = halogen, CN; X = O, two alkoxy groups OR23, C2-C10-alkylene-α,ω-dihydroxy group straight or branched chain, H/OR9, CH1OR11 where R23 = C1-C20-alkyl; R9 = H, or protecting group; R10, R11 = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, 5-7 membered carbocyclic ring; T-Y = OC(=O), OCH2, CH2C(=O), NR24C(=O), NR24SO2; R24 = H, C1-C10-alkyl; Z = O, H/OR12 where R12 = H or protecting group) were prepared in addition to all possible stereoisomers and mixts. Thus II was prepared from 2-methyl-4-thiazolecarboxaldehyde in a multistep synthesis. The IC50 of II was 5.1 nM on MCF-7 breast tumor and had an IC50 of 37 nM on the multidrug resistant carcinoma NCI/ADR.

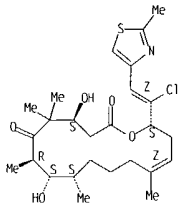
IT **289501-23-1P 289501-24-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 16-halogen epothilone derivs. for use as antitumor agents)

RN 289501-23-1 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1Z)-1-chloro-2-(2-methyl-4-

L5 ANSWER 55 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
thiazolyl)ethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-,
(4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

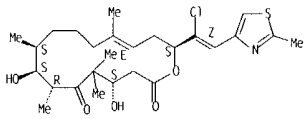
Absolute stereochemistry.
Double bond geometry as shown.



RN 289501-24-2 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1Z)-1-chloro-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



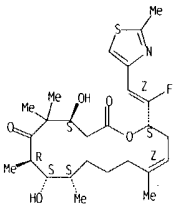
IT **289500-87-4P 289500-98-7P 289502-32-5P**
289502-36-9P 289502-65-4P 289502-69-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 16-halogen epothilone derivs. for use as antitumor agents)

RN 289500-87-4 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1Z)-1-fluoro-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 55 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

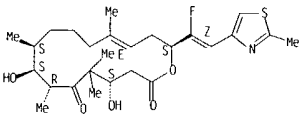
Absolute stereochemistry.
Double bond geometry as shown.



RN 289500-98-7 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1Z)-1-fluoro-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

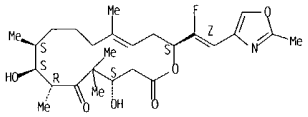


RN 289502-32-5 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1Z)-1-fluoro-2-(2-methyl-4-oxazolyl)ethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

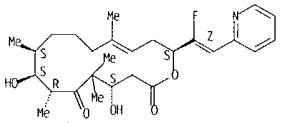
L5 ANSWER 55 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 289502-36-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1Z)-1-fluoro-2-(2-pyridinyl)ethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

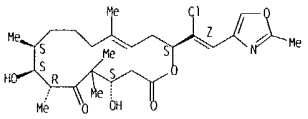
Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 289502-65-4 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1Z)-1-chloro-2-(2-methyl-4-oxazolyl)ethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

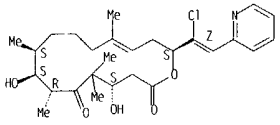


RN 289502-69-8 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1Z)-1-chloro-2-(2-pyridinyl)ethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

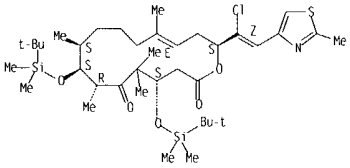
Absolute stereochemistry.
Double bond geometry as described by E or Z.

L5 ANSWER 55 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **289501-21-9P 289501-22-0P**
RL: RCT (Reactant): SPN (Synthetic preparation): PREP (Preparation): RACT (Reactant or reagent)
(preparation of 16-halogen epothilone derivs. for use as antitumor agents)
RN 289501-21-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1Z)-1-chloro-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

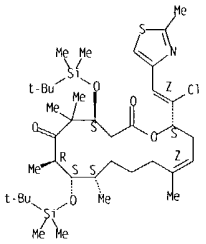
Absolute stereochemistry.
Double bond geometry as shown.



RN 289501-22-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1Z)-1-chloro-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 55 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L5 ANSWER 56 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:592720 CAPLUS
DOCUMENT NUMBER: 133:193027
TITLE: Preparation of new epothilone derivatives having pharmaceutical application as antitumor agents
INVENTOR(S): Klar, Ulrich; Schwede, Wolfgang; Buchmann, Bernd; Skuballa, Werner; Schirner, Michael; Grimm, Michael
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000049020	A2	20000824	WO 2000-EP1332	20000218 <--
WO 2000049020	A3	20001228		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19908763	A1	20000824	DE 1999-19908763	19990218 <--
PRIORITY APPLN. INFO.:			DE 1999-19908763 A	19990218

OTHER SOURCE(S): MARPAT 133:193027
GRAPHIC IMAGE:

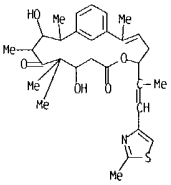
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
Epothilone derivs. I (R1a, R1b = H, C1-C10-alkyl, aryl, C7-C20-aralkyl; (CH2)m m = 1-5; CH2OCH2; R2a, R2b = H, C1-C10-alkyl, aryl, C7-C20-aralkyl; (CH2)n n = 2-5; E = A or B where t = 1-2, w = 1-2; G, G1 = H, halogen, CN, R24, C1-C20-acyl, C1-C20-acyloxy, OR24, CO2R24, N3, NO2, NR24aR24b; R24a, R24b = R24, (CH2)e e = 4-6; R24 = R3a = H, C1-C10-alkyl, aryl, C7-C20-aralkyl; R14 = H, OR14a, halogen; R3b = OPG14; R3b, R4a = bond; R4a, R4b = H, F, C1-C10-alkyl, aryl, C7-C20-aralkyl; R5 = H, C1-C10-alkyl, aryl, C7-C20-aralkyl, (CH2)s-A where s = 1-4, A = OR22, halogen; R22 = H, protecting group; R6,R7 = H, bond, O; R8 = H, F, C1-C10-alkyl, aryl, C7-C20-aralkyl; X = O, two alkoxy groups OR23, C2-C10-alkylene-α,ω-dihydroxy group straight or branched, H/OR9, CR10R11 where R23 = C1-C20-alkyl; R9 = H, protecting group; R10, R11 = H, C1-C10-alkyl, aryl, C7-C20-aralkyl or together are a 5-7 membered carbocyclic ring; Y = O or 2 H atoms; Z = O, H/OR12 where R12 = O, protecting group) were

L5 ANSWER 56 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

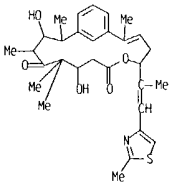
prepd. in addn. to all possible stereoisomers and mixts. Thus II was prepd. from 1,3-bis(hydroxymethyl)benzene in a multistep synthesis. These epothilone derivs. interact with tubulin by stabilizing the formed microtubule. The compds. are able to influence the cell division in a phase-specific manner and are suited for treating malignant tumors, for example, ovarian cancer, gastric carcinoma, colon cancer, breast cancer, lung cancer, head and neck cancer, malignant melanoma, and acute lymphocytic and myelocytic leukemia. These derivs. are suited for use in anti-angiogenic therapy as well as for treating chronic inflammatory diseases (psoriasis, arthritis). These compds. can be applied or incorporated in polymeric materials to prevent uncontrolled cell proliferations and to improve the compatibility of medical implants. They can be used alone or in conjunction with addnl. constituents and substance classes to achieve additive or synergistic effects in tumor therapy.

IT **289484-47-5P 289484-52-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of new epothilone derivs. for use as antitumor agents)
RN 289484-47-5 CAPLUS
CN 6-Oxabicyclo[13.3.1]nonadeca-1(19),2,15,17-tetraene-7,11-dione, 9,13-dihydroxy-2,10,10,12,14-pentamethyl-5-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (2Z,5S,9S,12R,13S,14S)- (9CI) (CA INDEX NAME)



RN 289484-52-2 CAPLUS
CN 6-Oxabicyclo[13.3.1]nonadeca-1(19),2,15,17-tetraene-7,11-dione, 9,13-dihydroxy-2,10,10,12,14-pentamethyl-5-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (2E,5S,9S,12R,13S,14S)- (9CI) (CA INDEX NAME)

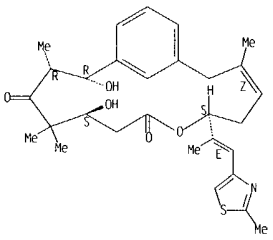
L5 ANSWER 56 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **289484-67-9P 289484-71-5P 289484-72-6P**
289484-77-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of new epothilone derivs. for use as antitumor agents)

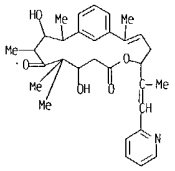
RN 289484-67-9 CAPLUS
CN 7-Oxabicyclo[13.3.1]nonadeca-1(19),3,15,17-tetraene-8,12-dione, 10,14-dihydroxy-3,11,11,13-tetramethyl-6-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (3Z,6S,10S,13R,14R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

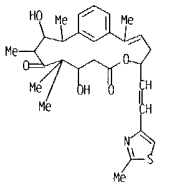


RN 289484-71-5 CAPLUS
CN 6-Oxabicyclo[13.3.1]nonadeca-1(19),2,15,17-tetraene-7,11-dione, 9,13-dihydroxy-2,10,10,12,14-pentamethyl-5-[(1E)-1-methyl-2-(2-

L5 ANSWER 56 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
pyridinyl)ethenyl]-, (2Z,5S,9S,12R,13S,14S)- (9CI) (CA INDEX NAME)

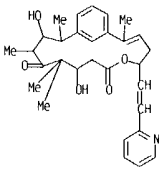


RN 289484-72-6 CAPLUS
CN 6-Oxabicyclo[13.3.1]nonadeca-1(19),2,15,17-tetraene-7,11-dione, 9,13-dihydroxy-2,10,10,12,14-pentamethyl-5-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (2Z,5S,9S,12R,13S,14S)- (9CI) (CA INDEX NAME)



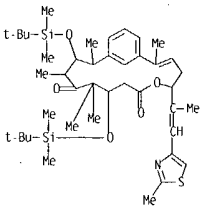
RN 289484-77-1 CAPLUS
CN 6-Oxabicyclo[13.3.1]nonadeca-1(19),2,15,17-tetraene-7,11-dione, 9,13-dihydroxy-2,10,10,12,14-pentamethyl-5-[(1E)-2-(2-pyridinyl)ethenyl]-, (2Z,5S,9S,12R,13S,14S)- (9CI) (CA INDEX NAME)

L5 ANSWER 56 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



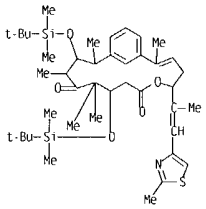
IT **289484-46-4P 289484-51-1P 289484-66-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of new epothilone derivs. for use as antitumor agents)

RN 289484-46-4 CAPLUS
CN 6-Oxabicyclo[13.3.1]nonadeca-1(19),2,15,17-tetraene-7,11-dione, 9,13-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10,10,12,14-pentamethyl-5-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (2Z,5S,9S,12R,13S,14S)- (9CI) (CA INDEX NAME)



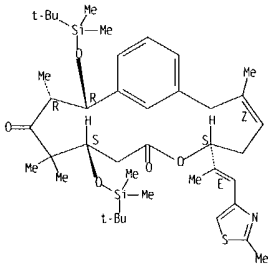
RN 289484-51-1 CAPLUS
CN 6-Oxabicyclo[13.3.1]nonadeca-1(19),2,15,17-tetraene-7,11-dione, 9,13-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,10,10,12,14-pentamethyl-5-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (2E,5S,9S,12R,13S,14S)- (9CI) (CA INDEX NAME)

L5 ANSWER 56 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 289484-66-8 CAPLUS
CN 7-Oxabicyclo[13.3.1]nonadeca-1(19),3,15,17-tetraene-8,12-dione, 10,14-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,11,11,13-tetramethyl-6-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (3Z,6S,10S,13R,14R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L5 ANSWER 57 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

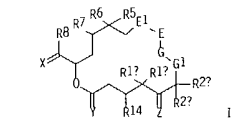
ACCESSION NUMBER: 2000:592719 CAPLUS
DOCUMENT NUMBER: 133:193025
TITLE: Preparation of new epothilone derivatives and their pharmaceutical uses
INVENTOR(S): Klar, Ulrich; Schwede, Wolfgang; Skuballa, Werner; Buchmann, Bernd; Schirner, Michael; Menrad, Andreas
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000049019	A2	20000824	WO 2000-EP1331	20000218 <--
WO 2000049019	A3	20010301		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19908760	A1	20000824	DE 1999-19908760	19990218 <--

PRIORITY APPLN. INFO.: DE 1999-19908760 A 19990218
OTHER SOURCE(S): MARPAT 133:193025
GRAPHIC IMAGE:



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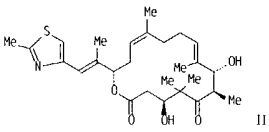


II

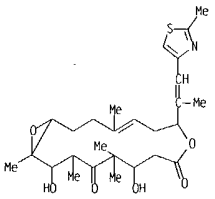
ABSTRACT:
Epothilone derivs. I (R1a, R1b = H, C1-C10 alkyl, aryl; C7-C20 aralkyl; or together are (CH2)m m = 1-5; or CH2OCH2; R2a, R2b = H, C1-C10 alkyl, aryl; C7-C20 aralkyl; or together are (CH2)n n = 2-5; G1-G-E-E1 = CR3aR3b-CR4=CH-CH2; CR3aR3b-CO(T)R4-CHO(T)-CH2; (2,3-epoxy)-CR3aR3b-CR4OCH-CH2; CR3aR3b-COH(H)R4-CHOH(H)-CH2; CR3a=CR4-CH=CH where R3a = H, C1-C10 alkyl, aryl; C7-C20 aralkyl; R14 = H, OR14a, halogen, OSO2R14b; R3b = OPG14 or R3b, R14a = bond; R4 = H, C1-C10 alkyl, aryl; C7-C20 aralkyl; R5 = H, C1-C10 alkyl, aryl; C7-C20 aralkyl, (CH2)s-A s = 1-4, A = OR22 or halogen; R22 = H or protecting group; R6, R7 = H, O, bond; R8 = H, C1-C10 alkyl, aryl; C7-C20 aralkyl; X = O, OR23, C2-C10-alkylene-α,ω-dihydroxy which can be a straight chain or branched; H/OR9 or the group CR10R11 where R23 = C1-C20 alkyl; R9 = H or a protecting group; R10,R11 = H, C1-C20 alkyl, aryl; C7-C20 aralkyl or R10,R11 together form a 5-7 membered carbocyclic ring; Y = O or 2 H atoms; Z = O or H/OR12 where R12 = H or a protecting group) were prepared in addition to all possible stereoisomers and mixts. Thus II was prepared from (±)-1-acetoxypentan-4-one in a multistep synthesis. These epothilone derivs. interact with tubulin by stabilizing the microtubuli which are formed. They are able to influence the cell division phase-specifically and are suitable for treating malignant tumors such as cancers of the ovaries, stomach, colon, glands, breasts, lungs, head and neck, malignant melanoma and acute lymphocytic and myelocytic leukemia. These compds. are also suitable for anti-angiogenesis therapy and for treating chronic inflammatory diseases (psoriasis, arthritis) and can be deposited on or in polymer materials in order to prevent uncontrolled cell proliferations on medical implants and to improve the compatibility. These derivs. can be used alone or in combination with other principles and classes of substances that can be used in the therapy of tumors

L5 ANSWER 57 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

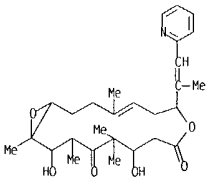
to achieve additive or synergistic effects.

IT **289477-95-8P 289478-09-7P 289482-00-4P**
289482-07-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of new epothilone derivs. and their pharmaceutical uses)

RN 289477-95-8 CAPLUS
CN 8,17-Dioxabicyclo[14.1.0]heptadec-4-ene-9,13-dione, 11,15-dihydroxy-4,12,12,14,16-pentamethyl-7-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4Z,7S,11S,14R,15R)- (9CI) (CA INDEX NAME)

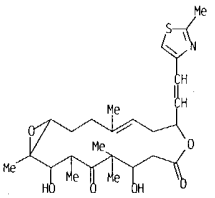


RN 289478-09-7 CAPLUS
CN 8,17-Dioxabicyclo[14.1.0]heptadec-4-ene-9,13-dione, 11,15-dihydroxy-4,12,12,14,16-pentamethyl-7-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4Z,7S,11S,14R,15R)- (9CI) (CA INDEX NAME)

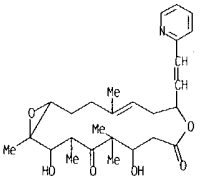


RN 289482-00-4 CAPLUS
CN 8,17-Dioxabicyclo[14.1.0]heptadec-4-ene-9,13-dione, 11,15-dihydroxy-4,12,12,14,16-pentamethyl-7-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (4Z,7S,11S,14R,15R)- (9CI) (CA INDEX NAME)

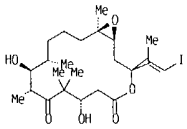
L5 ANSWER 57 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 289482-07-1 CAPLUS
CN 8,17-Dioxabicyclo[14.1.0]heptadec-4-ene-9,13-dione, 11,15-dihydroxy-4,12,12,14,16-pentamethyl-7-[(1E)-2-(2-pyridinyl)ethenyl]-, (4Z,7S,11S,14R,15R)- (9CI) (CA INDEX NAME)



L5 ANSWER 58 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:579172 CAPLUS
DOCUMENT NUMBER: 133:321735
TITLE: Total synthesis of 16-desmethylepothilone B, epothilone B10, epothilone F, and related side chain modified epothilone B analogues
AUTHOR(S): Nicolaou, K. C.; Hepworth, David; King, N. Paul; Finlay, M. Raymond V.; Scarpelli, Rita; Pereira, M. Manuela A.; Bollbuck, Birgit; Bigot, Antony; Werschkun, Barbara; Winssinger, Nicolas
CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Chemistry--A European Journal (2000), 6(15), 2783-2800
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:321735
GRAPHIC IMAGE:



I

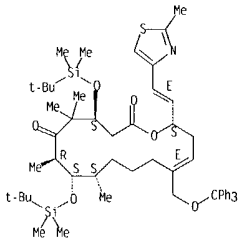
ABSTRACT:
The macrolactonization-based strategy for the total synthesis of epothilones has been streamlined and improved to a high level of efficiency and stereoselectivity. This strategy has been applied to the construction of vinyl iodide I which served as a common intermediate for the synthesis of a series of natural and designed epothilones including an epothilone B10, epothilone F, 16-desmethylepothilone B, pyridine epothilones, dimeric epothilones, and benzenoid epothilones.

IT **226940-49-4 226940-50-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of side chain modified epothilone B analogs)
RN 226940-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-

L5 ANSWER 58 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

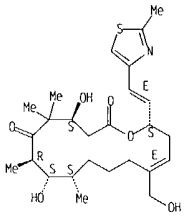
L5 ANSWER 58 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-13-[(triphenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 226940-50-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 59 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:573798 CAPLUS
DOCUMENT NUMBER: 133:177064
TITLE: Preparation of epothilone derivatives useful as pharmaceuticals
INVENTOR(S): Klar, Ulrich; Skuballa, Werner; Buchmann, Bernd; Schwede, Wolfgang; Schirner, Michael
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047584	A2	20000817	WO 2000-EP1104	20000211 <--
WO 2000047584	A3	20001228		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19907480	A1	20000817	DE 1999-19907480	19990211 <--
CA 2360952	AA	20000817	CA 2000-2360952	20000211 <--
EP 1161430	A2	20011212	EP 2000-920433	20000211 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008206	A	20020219	BR 2000-8206	20000211
JP 2002536450	T2	20021029	JP 2000-598504	20000211
EE 200100422	A	20021216	EE 2001-422	20000211
BG 105803	A	20020329	BG 2001-105803	20010809
NO 2001003900	A	20011011	NO 2001-3900	20010810 <--
ZA 2001007458	A	20021210	ZA 2001-7458	20010910

PRIORITY APPLN. INFO.: DE 1999-19907480 A 19990211
DE 1999-19954229 A 19991104
WO 2000-EP1104 W 20000211
OTHER SOURCE(S): MARPAT 133:177064
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

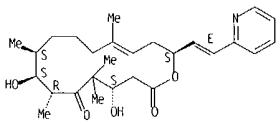
ABSTRACT:
Novel epothilone derivs. I (R4 = R5 = H, C1-C10 alkyl, aryl, C7-C20 aralkyl;

L5 ANSWER 59 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
R6, R7 are each H, or together an addnl. bond or O; R8 = Me or H; R1a, R1b together = trimethylene; R2 = Ph, CH2Ph; X = 2-pyridyl, 2-methyl-4-thiazolyl, 2-methyl-4-oxazolyl; or R1a, R1b together = trimethylene; R2 = Me, Et, Pr; X = 2-pyridyl, 2-methyl-4-thiazolyl, 2-methyl-4-oxazolyl; or simultaneously R1a = R1b = Me; R2 = Me, Et, Pr; X = 2-pyridyl, 2-methyl-4-thiazolyl or 2-methyl-4-oxazolyl; and the N and/or S atoms in X can be in an oxidized form; and if R2 and R8 = Me, X can only be a 2-pyridyl residue which is optionally oxidized at the nitrogen atom) and all possible stereoisomers and their mixts were prepd. Thus II was prepd. in a multistep sequence from the starting materials III and IV. The novel compds. interact with tubulin by stabilizing the formed microtubuli. The compds. are able to influence the cell division in a phase-specific manner and are suited for treating malignant tumors, for example, ovarian cancer, gastric carcinoma, colon cancer, breast cancer, lung cancer, head and neck cancer, malignant melanoma, and acute lymphocytic and myelocytic leukemia. The inventive compds. are suited for use in anti-angiogenic therapy as well as for treating chronic inflammatory diseases (psoriasis, arthritis). In order to prevent uncontrolled cell proliferations and to improve the compatibility of medical implants, the inventive compds. can be applied or incorporated in polymeric materials. The inventive compds. can be used alone or, in order to achieve additive or synergistic effects, in conjunction with addnl. constituents and substance classes which can be use in tumor therapy.

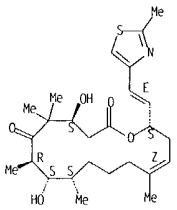
IT **252986-93-9P 288386-51-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of epothilone derivs. useful as pharmaceuticals)
RN 252986-93-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 59 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

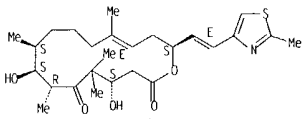


L5 ANSWER 59 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 288386-51-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **288387-16-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilone derivs. useful as pharmaceuticals)
RN 288387-16-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

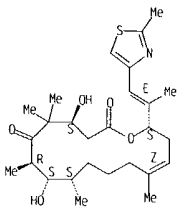
L5 ANSWER 60 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:555968 CAPLUS
DOCUMENT NUMBER: 133:275843
TITLE: Epothilone A-D and their thiazole-modified analogs as novel anticancer agents
AUTHOR(S): Hofle, G.; Glaser, N.; Leibold, T.; Sefkow, M.
CORPORATE SOURCE: Dep. Nat. Product Chem., GBF, Gesellschaft Biotechnol. Forschung mbH, Braunschweig, D-38124, Germany
SOURCE: Pure and Applied Chemistry (1999), 71(11), 2019-2024
CODEN: PACHAS; ISSN: 0033-4545
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Starting from epothilone A-D obtained by large scale fermentation of the myxobacterium Sorangium cellulosum, the thiazole side-chain was extensively modified by substitution, oxidation and replacement. Metalation afforded the C-19 carbanion which was quenched by various carbon and heteroatom electrophiles to give C-19 substituted epothilones. Thiazole N-oxides were obtained by treatment of epothilone A and B with m-chloroperbenzoic acid and rearranged by acetic anhydride to 21-acetoxy epothilones. Cleavage of epothilones A and B with ozone gave Me ketones from which carbonyl derivs. and aldol condensation products were prepared. Similarly vinyl boronic acid was obtained and transformed by Suzuki coupling or iodination/Stille coupling to aryl and heteroaryl analogs. The structure-activity relationships for thiazolyl side chain of epothilones were in line with published data obtained from analogs prepared by total synthesis. Only few modifications were tolerated without significant loss of activity, i.e. replacement of the thiazole by an oxazole ring or introduction of small substituents at C-21.

IT **189453-10-9P**, Epothilone D
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(preparation of epothilone A-D and their thiazole-modified analogs as anticancer agents)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

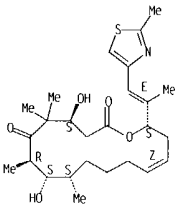
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 60 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **186692-73-9P**, Epothilone C
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilone A-D and their thiazole-modified analogs as anticancer agents)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

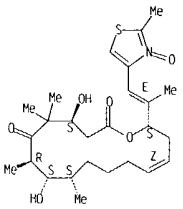
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **246520-37-6P**

L5 ANSWER 60 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of epothilone A-D and their thiazole-modified analogs as anticancer agents)
RN 246520-37-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-3-oxido-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

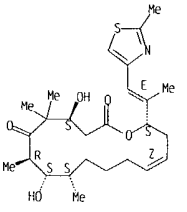


REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 61 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:514331 CAPLUS
DOCUMENT NUMBER: 134:100671
TITLE: Chapter I: The first total syntheses of epothilones A, B, C and D. Chapter II: The first total syntheses of 12-epi-CP-263,114, and 12-epi-CP-225,917
AUTHOR(S): Meng, Dongfang
CORPORATE SOURCE: Columbia University, USA
SOURCE: (**1999**) 326 pp. Avail.: University Microfilms International, Order No. DA9949022 From: Diss. Abstr. Int., B 2000, 60(10), 5096
DOCUMENT TYPE: Dissertation
LANGUAGE: English
ABSTRACT: Unavailable
IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: SPN (Synthetic preparation); PREP (Preparation)
(total syntheses of epothilones A, B, C and D)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

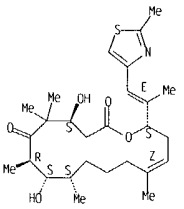
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



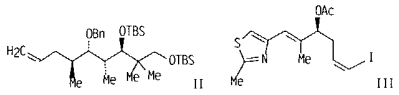
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 61 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L5 ANSWER 62 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:514132 CAPLUS
DOCUMENT NUMBER: 133:266631
TITLE: Total Synthesis of Epothilone A
AUTHOR(S): Zhu, Bin; Panek, James S.
CORPORATE SOURCE: Department of Chemistry and the Center for Streamlined Synthesis Metcalf Center for Science and Engineering, Boston University, Boston, MA, 02215, USA
SOURCE: Organic Letters (2000), 2(17), 2575-2578
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:266631
GRAPHIC IMAGE:

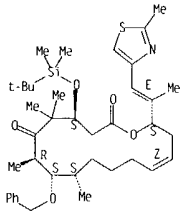


ABSTRACT:
Epothilones A (I) and B are potent antitumor natural products with a Taxol-like mechanism of action. A total synthesis of I is reported, which utilized chiral silane-based bond construction methodol. to introduce the key C-6 and C-7 stereocenters of fragment (II). The C-15 stereocenter of fragment (III) was established by a lipase-mediated kinetic resolution The fragments were assembled with a Suzuki coupling reaction and an aldol condensation and cyclized with a Yamaguchi-type macrolactonization reaction.

IT **186692-73-9P 187283-49-4P 297131-86-3P**
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of epothilone A)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

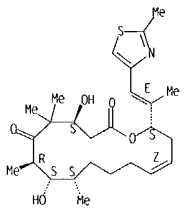
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 62 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



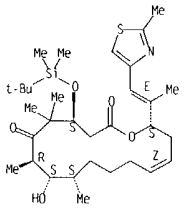
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 62 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 187283-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 297131-86-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-8-(phenylmethoxy)-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 63 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:368562 CAPLUS
DOCUMENT NUMBER: 133:27369
TITLE: Epothilone and epothilone derivatives production based on recombinant nucleic acids encoding the epithilone polyketide synthase from Sorangium cellulosum
INVENTOR(S): Julien, Bryan; Katz, Leonard; Khosla, Chaitan; Tang, Li; Ziermann, Rainer
PATENT ASSIGNEE(S): Kosan Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031247	A2	20000602	WO 1999-US27438	19991119 <--
WO 2000031247	A3	20001207		
W: AL, AM, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, IL, IS, JP, KG, KP, KR, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1135470	A2	20010926	EP 1999-960500	19991119 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002530107	T2	20020917	JP 2000-584057	19991119
AU 768220	B2	20031204	AU 2000-17377	19991119
US 6410301	B1	20020625	US 2000-560367	20000428
US 2003096381	A1	20030522	US 2002-191694	20020708

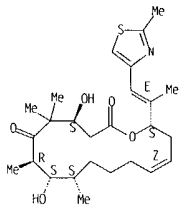
PRIORITY APPLN. INFO.: US 1998-109401P P 19981120
US 1999-119386P P 19990210
US 1999-122620P P 19990303
US 1999-130560P P 19990422
US 1999-443501 A2 19991119
WO 1999-US27438 W 19991119
US 2000-560367 A1 20000428
OTHER SOURCE(S): MARPAT 133:27369

ABSTRACT:
Recombinant genomic nucleic acids that encode all or a portion of the epothilone polyketide synthase (PKS) from Sorangium cellulosum SMP44 are provided. The epo gene cluster comprises 71,989 bp encoding the loading domain (epoA), the non-ribosomal peptide synthase (NRPS, module 1, epoB), each of the remaining 8 modules of the epothilone synthase module (epoC, epoD, epoE, and epoF), and the epoK gene that encodes a cytochrome P 450-like epoxidn. enzyme. Recombinant PKS genes are expressed in host cells for the production of epothilones, epothilone derivs., and polyketides that are useful as cancer chemotherapeutics, fungicides, and immunosuppressants. Two hybrid PKS enzymes

L5 ANSWER 63 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
are hybrids of deoxyerythronolide B synthase (DEBS) and epothilone NRPS module. The first hybrid PKS is composed of 4 proteins: DEBS1: a fusion protein composed of the ketosynthase (KS) domain of module 3 of DEBS and all but the KS domain of the loading domain of the epothilone PKS; the epothilone NRPS module; and a fusion protein composed of the KS domain of module 2 of the epothilone PKS fused to the acyltransferase domain of module 5 of DEBS and the rest of DEBS3. The second hybrid PKS is composed of 5 proteins: DEBS1, a fusion protein composed of the KS domain of module 3 of DEBS and all but the KS domain of the epothilone PKS loading domain; the epothilone NRPS module; a fusion protein composed of the KS domain of module 2 of epothilone PKS fused to the AT domain of module 4 of DEBS and the ret of DEBS2; and DEBS3. Novel epithilone derivs. are produced where these hybrid PKS are expressed in Streptomyces coelicolor or Saccharopolyspora erythraea.

IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(epothilone and epothilone derivs. production based on recombinant nucleic acids encoding the epithilone polyketide synthase from Sorangium cellulosum)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

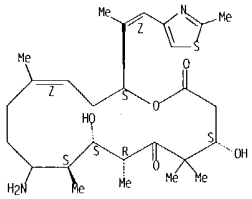
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

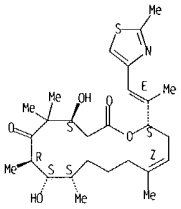
L5 ANSWER 63 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 272114-15-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 10-amino-4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1Z)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



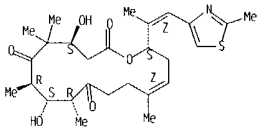
L5 ANSWER 63 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **272114-14-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(epothilone and epothilone derivs. production based on recombinant nucleic acids encoding the epithilone polyketide synthase from Sorangium cellulosum)
RN 272114-14-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6,10-trione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1Z)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13Z,16S)-(9CI) (CA INDEX NAME)

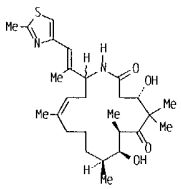
Absolute stereochemistry.
Double bond geometry as shown.



IT **272114-15-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(epothilone and epothilone derivs. production based on recombinant nucleic acids encoding the epithilone polyketide synthase from Sorangium cellulosum)

L5 ANSWER 64 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2000:345686 CAPLUS
DOCUMENT NUMBER:	133:58659
TITLE:	On the Total Synthesis and Preliminary Biological Evaluations of 15(R) and 15(S) Aza-dEpoB: A Mitsunobu Inversion at C15 in Pre-Epothilone Fragments
AUTHOR(S):	Stachel, Shawn J.; Chappell, Mark D.; Lee, Chul Bom; Danishefsky, Samuel J.; Chou, Ting-Chao; Horwitz, Susan B.
CORPORATE SOURCE:	Laboratories for Bioorganic Chemistry and Biochemical Pharmacology, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE:	Organic Letters (2000), 2(11), 1637-1639 CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 133:58659
GRAPHIC IMAGE:	



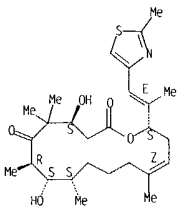
I

ABSTRACT:
The syntheses of two epothilone analogs, 15(S)-aza-12,13-desoxyepothilone B (I) (R = α-H) and the epimeric 15(R)-aza-12,13-desoxyepothilone B I (R = β-H), are described. A Mitsunobu inversion was utilized for elaboration of pre-epothilone fragments to the corresponding macrolactam. Tubulin binding and cytotoxicity profiles of I are presented.

IT **189453-10-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antitumor activity of)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 64 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 65 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

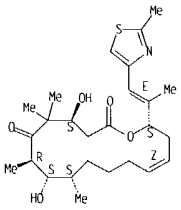
ACCESSION NUMBER: 2000:316343 CAPLUS
Correction of: 1997:528752
DOCUMENT NUMBER: 132:293587
Correction of: 127:149021
TITLE: The Olefin Metathesis Approach to Epothilone A and Its Analogs
AUTHOR(S): Nicolaou, K. C.; He, Y.; Vourloumis, D.; Vallberg, H.; Roschangar, F.; Sarabia, F.; Ninkovic, S.; Yang, Z.; Trujillo, J. I.
CORPORATE SOURCE: Institute for Chemical Biology, La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (1997), 119(34), 7960-7973
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
The olefin metathesis approach to epothilone A (I) and several diastereomeric analogs is described. Key building blocks II, (S)-OHCCH(Me)CH2CH2CH2CH=CH2, and (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CO2H were constructed in optically active form and were coupled and elaborated to olefin metathesis precursor III (R = SiMe2CMe3) via an aldol reaction and an esterification coupling. Olefin metathesis of compound III (R = SiMe2CMe3), under the catalytic influence of RuCl2(:CHPh)(PCy3)2, furnished cis- and trans-cyclic olefins IV (R = SiMe2CMe3). Epoxidn. of (Z)-IV (R = H) gave I and several analogs, whereas epoxidn. of (E)-IV (R = H) resulted in addnl. epothilones. Similar elaboration of isomeric as well as simpler intermediates resulted in yet another series of epothilone analogs and model systems.

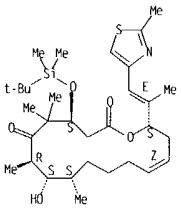
IT **186692-73-9P 187283-49-4P 187283-52-9P**
188260-10-8P 193071-85-1P 193071-86-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilone A and analogs via olefin metathesis)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

L5 ANSWER 65 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 187283-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

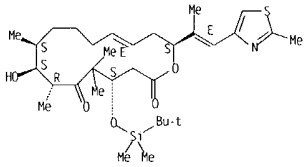
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 187283-52-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

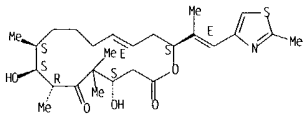
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 65 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

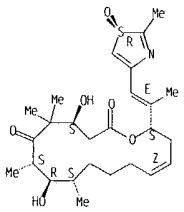
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 193071-85-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[(1R)-2-methyl-1-oxido-4-thiazolyl]ethenyl]-, (4S,7S,8R,9S,13Z,16S)- (9CI) (CA INDEX NAME)

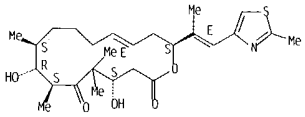
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 65 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 193071-86-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

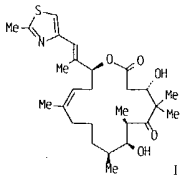


IT **193071-80-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of epothilone A and analogs via olefin metathesis)
RN 193071-80-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[(1R)-2-methyl-1-oxido-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 66 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:309568 CAPLUS
DOCUMENT NUMBER: 133:89354
TITLE: En Route to a Plant Scale Synthesis of the Promising Antitumor Agent 12,13-Desoxyepothilone B
AUTHOR(S): Chappell, Mark D.; Stachel, Shawn J.; Lee, Chul Bom; Danishefsky, Samuel J.
CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Organic Letters (2000), 2(11), 1633-1636
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:89354
GRAPHIC IMAGE:



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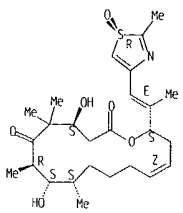
ABSTRACT:
Efficient and processable syntheses of key building blocks, I and (S)-H2C:CHCH2CHMeCHO, of the antitumor agent 12,13-desoxyepothilone B (II) by catalytic asym. induction are herein described.

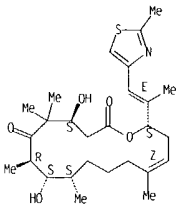
IT **189453-10-9P**, 12,13-Desoxyepothilone B
RL: PNU (Preparation, unclassified); PREP (Preparation)
(syntheses of key building blocks en route to a plant scale synthesis of 12,13-desoxyepothilone B)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 65 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

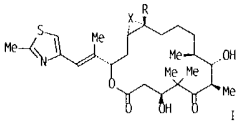


L5 ANSWER 66 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 67 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:273850 CAPLUS
DOCUMENT NUMBER: 133:30608
TITLE: Synthesis, Structure Proof, and Biological Activity of Epothilone Cyclopropanes
AUTHOR(S): Johnson, James; Kim, Soong-Hoon; Bifano, Marc; DiMarco, John; Fairchild, Craig; Gougoutas, Jack; Lee, Francis; Long, Byron; Tokarski, John; Vite, Gregory
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543-4000, USA
SOURCE: Organic Letters (2000), 2(11), 1537-1540
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:30608
GRAPHIC IMAGE:

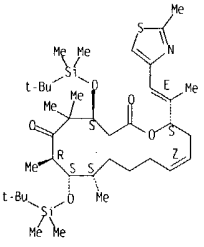


ABSTRACT:
A semisynthetic route to epothilone cyclopropanes from epothilones A (I; X = O, R = H) and B (I; X = O, R = Me) is described. Of significance, the deoxygenation of the 12,13-epoxide to give the corresponding olefin was achieved with high efficiency. The title compds. I (X = CH2, R = H) and I (R = Me) were active in both tubulin polymerization and cytotoxicity assays, which is in direct contrast to a previously published report. These results provide further evidence that the role of the 12,13-epoxide of epothilones is largely conformational and argue against some of the current pharmacophore models.

IT **186692-73-9P**, Epothilone C
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, structure proof, and biol. activity of epothilone cyclopropanes)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

L5 ANSWER 67 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, structure proof, and biol. activity of epothilone cyclopropanes)
RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

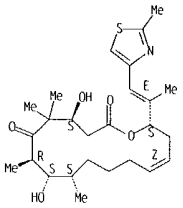
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

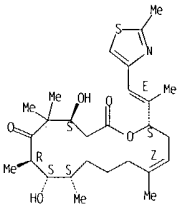
L5 ANSWER 67 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **189453-10-9P**, Epothilone D
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(synthesis, structure proof, and biol. activity of epothilone cyclopropanes)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



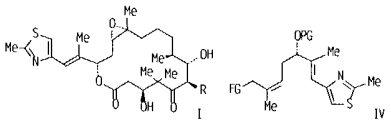
IT **186692-84-2P**

L5 ANSWER 68 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:254124 CAPLUS
DOCUMENT NUMBER: 132:293600
TITLE: An efficient procedure for the synthesis of epothilone B, derivatives, and its intermediates
INVENTOR(S): Mulzer, Johann; Mantoulidis, Andreas; Oehler, Elisabeth
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 32 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19848306	A1	20000420	DE 1998-19848306	19981014 <--
CA 2346493	AA	20000427	CA 1999-2346493	19991014 <--
WO 2000023452	A1	20000427	WO 1999-EP7746	19991014 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9964717	A1	20000508	AU 1999-64717	19991014 <--
AU 763717	B2	20030731		
EP 1121364	A1	20010808	EP 1999-952569	19991014 <--
EP 1121364	B1	20030108		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002527521	T2	20020827	JP 2000-577178	19991014
AT 230751	E	20030115	AT 1999-952569	19991014
PT 1121364	T	20030430	PT 1999-952569	19991014
ES 2189508	T3	20030701	ES 1999-952569	19991014
US 6605726	B1	20030812	US 2001-807370	20010601
US 2003220503	A1	20031127	US 2003-420716	20030423

PRIORITY APPLN. INFO.: DE 1998-19848306 A 19981014
WO 1999-EP7746 W 19991014
US 2001-807370 A3 20010601
OTHER SOURCE(S): CASREACT 132:293600; MARPAT 132:293600
GRAPHIC IMAGE:

L5 ANSWER 68 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



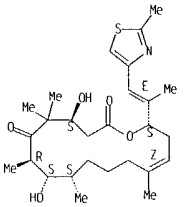
I IV

ABSTRACT:
A new procedure for the production of epothilone B and its derivs. (I) (R = alkyl, cycloalkyl, aryl, heteroaryl, methylaryl, etc.) including its intermediates is reported. The method is based upon the stereoselective synthesis of three key structural fragments. C1-C6 (II) (S)-PGO(CH2)2CH(OPG)CMe2COCH2R, C7-C10 (III) (S)-PGOCH2CH(Me)CH2CH2FG. (PG = hydroxyl protecting group, such as TBDMS, etc. ; FG = SO2Ph, I, etc.), and C11-C20 (IV) starting with D-valine. TBDPS protected (2S)-methylpropan-1,3-diol and (S)-3-hydroxybutyrolactone, resp. The product, obtained after coupling of III and IV, on reaction with II formed an intermediate which on macrocyclization produced I.

IT **189453-10-9P**, Epothilone D **189453-35-8P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilone B, derivs., and its intermediates)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

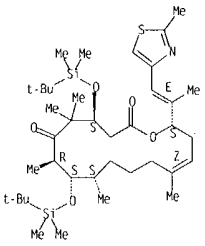
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 68 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 69 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

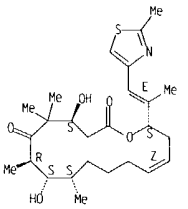
ACCESSION NUMBER: 2000:88787 CAPLUS
DOCUMENT NUMBER: 132:289462
TITLE: Cloning and heterologous expression of the epothilone gene cluster
AUTHOR(S): Tang, Li; Shah, Sanjay; Chung, Loleta; Carney, John; Katz, Leonard; Khosla, Chaitan; Julien, Bryan
CORPORATE SOURCE: KOSAN Biosciences, Hayward, CA, 94545, USA
SOURCE: Science (Washington, D. C.) (**2000**), 287(5453), 640-642
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English

ABSTRACT:
The polyketide epothilone is a potential anticancer agent that stabilizes microtubules in a similar manner to Taxol. The gene cluster responsible for epothilone biosynthesis in the myxobacterium Sorangium cellulosum was cloned and completely sequenced. It encodes six multifunctional proteins composed of a loading module, one nonribosomal peptide synthetase module, eight polyketide synthase modules, and a P 450 epoxidase that converts desoxyepothilone into epothilone. Concomitant expression of these genes in the actinomycete Streptomyces coelicolor produced epothilones A and B. Streptomyces coelicolor is more amenable to strain improvement and grows about 10-fold as rapidly as the natural producer, so this heterologous expression system portends a plentiful supply of this important agent.

IT **186692-73-9**, Epothilone C **189453-10-9**, Epothilone D
RL: dPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(sequence and heterologous expression of epothilone gene cluster of Sorangium cellulosum)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

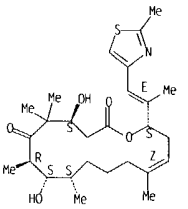
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 69 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



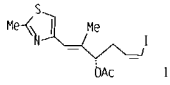
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

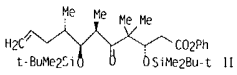


REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

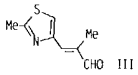
L5 ANSWER 70 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:52387 CAPLUS
DOCUMENT NUMBER: 132:251011
TITLE: Enantioselective total synthesis of epothilone A using multifunctional asymmetric catalyses
AUTHOR(S): Sawada, Daisuke; Shibasaki, Masakatsu
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, 113-0033, Japan
SOURCE: Angewandte Chemie, International Edition (2000), 39(1), 209-213
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:251011
GRAPHIC IMAGE:



I



II

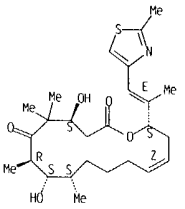


III

ABSTRACT:
The enantioselective total synthesis of epothilone A was achieved via the catalytic coupling of I and II. The key step in the preparation of I was the catalytic cyanosilylation of III. II was prepared via a catalytic organic acetalization followed by an aldol reaction.

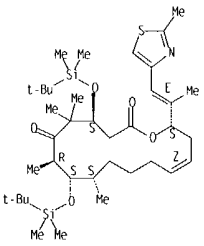
IT **186692-73-9P 186692-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enantioselective total synthesis of epothilone A)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS

L5 ANSWER 70 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 71 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:15195 CAPLUS
DOCUMENT NUMBER: 132:64110
TITLE: The preparation process, intermediate products and pharmaceutical use of epothilone derivatives
INVENTOR(S): Buchmann, Bernd; Klar, Ulrich; Skuballa, Werner; Schwede, Wolfgang; Schirner, Michael; Menrad, Andreas
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000485	A1	20000106	WO 1999-EP4915	19990630 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19830060	A1	20000210	DE 1998-19830060	19980630 <--
DE 19923001	A1	20001116	DE 1999-19923001	19990513 <--
AU 9950369	A1	20000117	AU 1999-50369	19990630 <--

PRIORITY APPLN. INFO.: DE 1998-19830060 A 19980630
DE 1999-19923001 A 19990513
WO 1999-EP4915 W 19990630
OTHER SOURCE(S): CASREACT 132:64110; MARPAT 132:64110
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

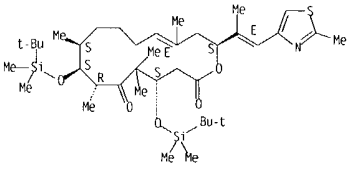
ABSTRACT:
The invention relates to new epothilone derivs. I [R1a, R1b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R1aR1b = (CH2)m, m = 2 - 5; R2a, R2b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R2aR2b = (CH2)n, n = 2 - 5; R3 = H, C1-10-alkyl, aryl, C7-10-aralkyl; R4a, R4b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R4aR4b = (CH2)m, m = 2 - 5; D-E = CH2CH2, CH:CH, C.tplbond.C, oxirane ring, CH(OH)CH(OH), CH(OH)CH2; R5 = C1-10-alkyl, aryl, C7-10-aralkyl; R6, R7 = H; R6R7 = O, bond; R8 = C1-10-alkyl, aryl, C7-10-aralkyl; R25 = H, C1-10-alkyl, C1-10-hydroxyalkyl, C1-10-haloalkyl; X = O, (OR9)2, C2-10-alkylene-α,ω-dioxy, CR11R12; CX = CH(OR10); R9 = C1-20-alkyl; R10 = H, protecting group; R11, R12 = H, C1-10-alkyl, aryl, C7-10-aralkyl; R11R12 = CH2,

L5 ANSWER 71 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
C5-7-carbocyclic ring; Y = O, CY = CH2; CZ = CH(OR13), R13 = H, protecting group] which are prepd. via cyclization of ketones II [R15 = H, OH halogen, OR15a, OSO2R15b; R15a = H, SO2-alkyl, SO2-aryl, SO2-aralkyl, (CH2)o, CR16aR16b; R15b = H, C1-20-alkyl, aryl, C7-20-aralkyl; R16a, R16b = H, C1-10-alkyl, aryl, C7-20-aralkyl; R16aR16b = (CH2)q; o = 2 - 4; q = 3 - 6]. Thus, epothilone deriv. III was prepd. via macrolactonization of carboxylic acid IV with 2,4,6-trichlorobenzoyl chloride and Et3N in THF followed by deprotection with aq. CF3CO2H in CH2Cl2. I cooperate with tubulin by stabilizing formed microtubuli.

IT **253448-16-7P 253448-18-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and pharmaceutical use of epothilone derivs.)

RN 253448-16-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

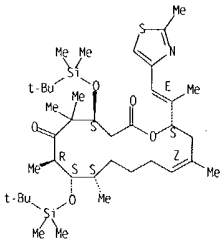
Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 253448-18-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

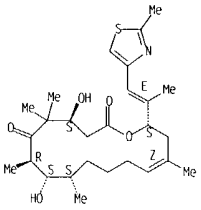
L5 ANSWER 71 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **253447-39-1P 253447-42-6P 253447-56-2P**
253447-59-5P 253447-62-0P 253447-68-6P
253447-71-1P 253447-74-4P 253447-77-7P
253447-83-5P 253447-86-8P 253448-19-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and pharmaceutical use of epothilone derivs.)

RN 253447-39-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

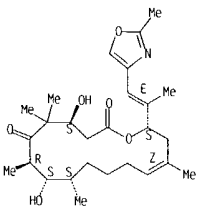
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 71 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

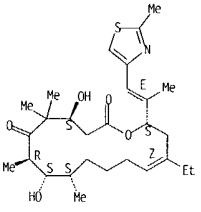
RN 253447-42-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 253447-56-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

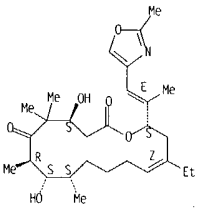
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 253447-59-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

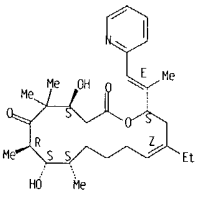
L5 ANSWER 71 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.
Double bond geometry as shown.



RN 253447-62-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

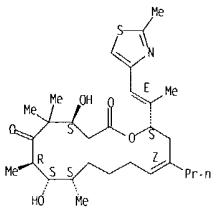
Absolute stereochemistry.
Double bond geometry as shown.



RN 253447-68-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-14-propyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

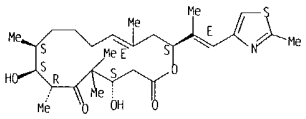
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 71 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 253447-71-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.

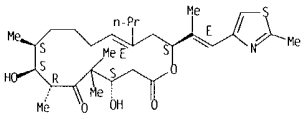


RN 253447-74-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

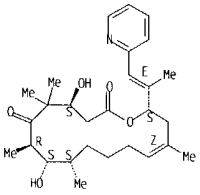
L5 ANSWER 71 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



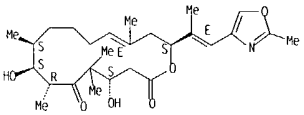
RN 253448-19-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



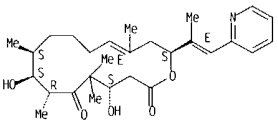
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 71 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



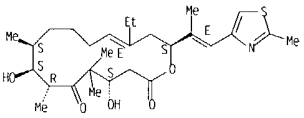
RN 253447-77-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 253447-83-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 14-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as described by E or Z.



RN 253447-86-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-14-propyl-.

L5 ANSWER 72 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:819379 CAPLUS
DOCUMENT NUMBER: 132:49832
TITLE: Preparation of 16-desmethylepothilones for the treatment of proliferative diseases.
INVENTOR(S): Nicolaou, Kyriacos Costa; Hepworth, David; Finlay, Maurice Raymond Verschoyle; King, Nigel Paul
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Scripps Research Institute
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967253	A2	19991229	WO 1999-EP4299	19990621 <--
WO 9967253	A3	20000420		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6380394	B1	20020430	US 1998-102602	19980622
AU 9947752	A1	20000110	AU 1999-47752	19990621 <--

PRIORITY APPLN. INFO.:
US 1998-102602 A 19980622
US 1999-123155P P 19990306
US 1999-124653P P 19990316
US 1996-32864P P 19961213
US 1997-856533 B1 19970514
US 1997-923869 A2 19970904
WO 1999-EP4299 W 19990621

OTHER SOURCE(S): CASREACT 132:49832; MARPAT 132:49832
GRAPHIC IMAGE:

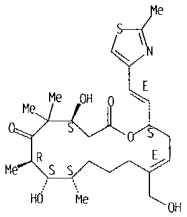
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
The invention relates to compds. I [X = bond, O; O = OH, I, H], and methods of synthesis of I, as well as for the synthesis of epothilone B (II) and their intermediates. Thus, 16-desmethyldesoxyepothilone analog III was prepared via Yamaguchi macrolactonization of hydroxy acid IV. The compds. I can be used

L5 ANSWER 72 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
e.g. in the treatment of proliferative diseases.

IT **226940-50-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 16-desmethylepothilones for the treatment of proliferative diseases.)
RN 226940-50-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

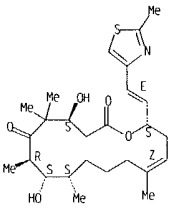
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **252986-93-9P**, 16-Desmethyl-12,13-deoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 16-desmethylepothilones for the treatment of proliferative diseases.)
RN 252986-93-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

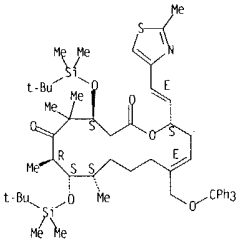
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 72 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **226940-49-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 16-desmethylepothilones for the treatment of proliferative diseases.)
RN 226940-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-13-[(triphenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 72 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

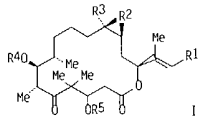
L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:819378 CAPLUS
DOCUMENT NUMBER: 132:49831
TITLE: Synthesis of epothilone derivatives and their use against proliferative diseases
INVENTOR(S): Nicolaou, Kyriacos Costa; King, Nigel Paul; Finlay, Maurice Raymond Verschoyle; He, Yun; Roschangar, Frank; Vourloumis, Dionisios; Vallberg, Hans; Bigot, Antony
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Scripps Research Institute; et al.
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967252	A2	19991229	WO 1999-EP4287	19990621 <--
WO 9967252	A3	20000316		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6380394	B1	20020430	US 1998-102602	19980622
CA 2334342	AA	19991229	CA 1999-2334342	19990621 <--
AU 9947748	A1	20000110	AU 1999-47748	19990621 <--
AU 757854	B2	20030306		
BR 9911420	A	20010320	BR 1999-11420	19990621 <--
EP 1089998	A2	20010411	EP 1999-931120	19990621 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
JP 2002518504	T2	20020625	JP 2000-555904	19990621
NZ 508622	A	20030725	NZ 1999-508622	19990621
RU 2227142	C2	20040420	RU 2000-132188	19990621
NO 2000006378	A	20010221	NO 2000-6378	20001214 <--
US 6531497	B1	20030311	US 2001-720070	20010419
US 2003203938	A1	20031030	US 2003-386999	20030311

PRIORITY APPLN. INFO.:
US 1998-102602 A 19980622
US 1996-32864P P 19961213
US 1997-856533 B1 19970514
US 1997-923869 A2 19970904
WO 1999-EP4287 W 19990621
US 2001-720070 A3 20010419

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
OTHER SOURCE(S): CASREACT 132:49831; MARPAT 132:49831
GRAPHIC IMAGE:



I

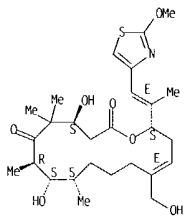
ABSTRACT:
The invention relates to epothilone analogs I [R1 = (un)substituted imidazol-2-yl, imidazol-4-yl, imidazol-5-yl, 2-substituted 1,3-thiazol-4-yl, (un)methylated 2-pyridyl group; R2 = O, bond; R3 = H, Me, Et, Pr, CHMe2, Bu, CH2CHMe2, CMe3, pentyl, hexyl, -CH=CH2, -C.tplbond.CH, -CH2F, -CH2Cl, -CH2OH, -CH2O(C1-C6-alkyl), CH2OMe, -CH2-S-(C1-C6-alkyl), CH2SMe; R4, R5 = H, Me, protecting group] or a salt of I where a salt-forming group is present. A further aspect of the invention is related to the synthesis of epothilone E [I; R1 = 2-(hydroxymethyl)-1,3-thiazol-4-yl, R2 = O, R3 - R5 = H] via coupling of iodide I (R1 = I, R2 = bond, R3 - R5 = H) with 2-(hydroxymethyl)-4-(tributylstannyl)thiazole in DMF containing catalytic Pd(MeCN)2Cl2 followed by stereoselective epoxidn. of the ring double bond with in situ generated MeC(:NH)O2H. These compds. have inter alia microtubuli depolymn. inhibiting activity and are useful against proliferative diseases.

IT **204513-12-2P**, Deoxyepothilone E **240816-04-0P**
240816-05-1P 240816-06-2P 240816-08-4P
240816-10-8P 252981-50-3P, Deoxyepothilone F
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of epothilones and derivs. and their use against proliferative diseases)

RN 204513-12-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

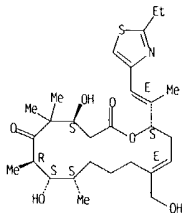
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-06-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethyl-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

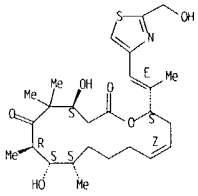
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-08-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethenyl-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

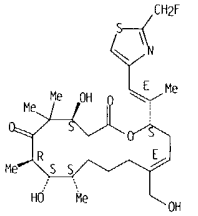
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-04-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

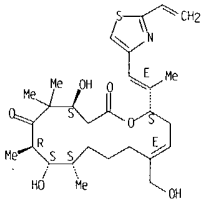
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-05-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-16-[(1E)-2-(2-methoxy-4-thiazolyl)-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

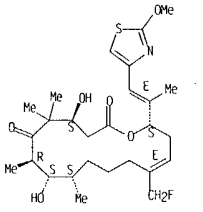
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(fluoromethyl)-4,8-dihydroxy-16-[(1E)-2-(2-methoxy-4-thiazolyl)-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

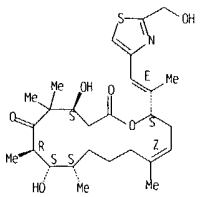
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 252981-50-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



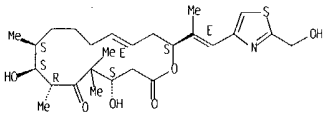
IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
204513-14-4P **204513-40-6P** **204513-50-8P**
209260-91-3P **209260-97-9P** **240816-07-3P**
240816-09-5P **240816-11-9P** **240816-12-0P**
240816-36-8P **240816-38-0P** **252981-40-1P**
252981-41-2P **252981-42-3P** **252981-43-4P**
252981-44-5P **252981-45-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of epothilones and derivs. and their use against proliferative diseases)

RN 186692-73-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

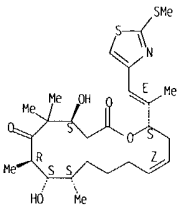
L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-40-6 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

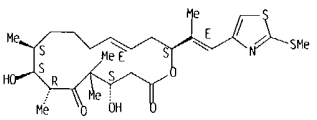
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-50-8 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

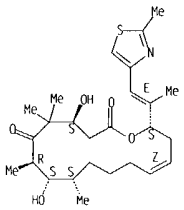
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-91-3 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-.

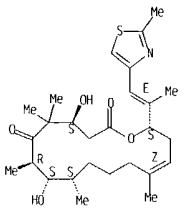
L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-10-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



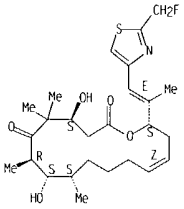
RN 204513-14-4 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

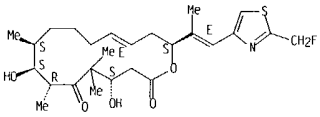
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-97-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

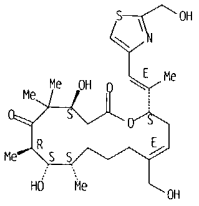


RN 240816-07-3 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

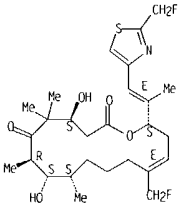
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-09-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(fluoromethyl)-16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

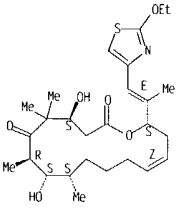
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-11-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethyl-4-thiazolyl)-1-methylethenyl]-13-(fluoromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

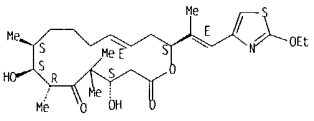
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-38-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethoxy-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

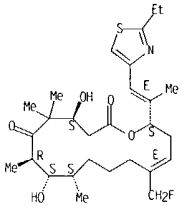
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 252981-40-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

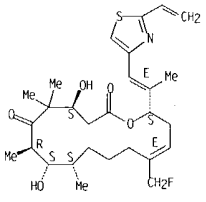
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-12-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethenyl-4-thiazolyl)-1-methylethenyl]-13-(fluoromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

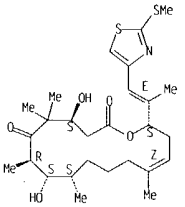
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-36-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethoxy-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

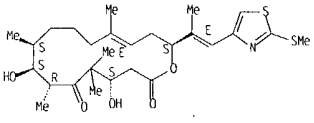
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 252981-41-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

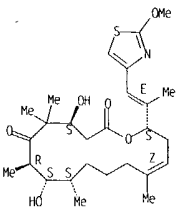
Absolute stereochemistry.
Double bond geometry as shown.



RN 252981-42-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-(2-methoxy-4-thiazolyl)-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

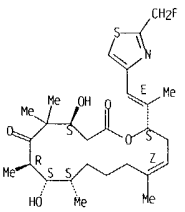
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 252981-43-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

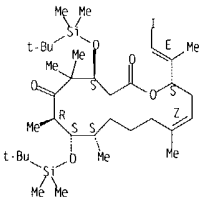
Absolute stereochemistry.
Double bond geometry as shown.



RN 252981-44-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethenyl-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

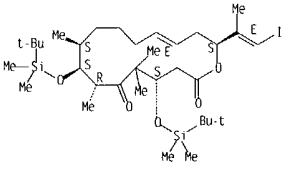
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 252981-56-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

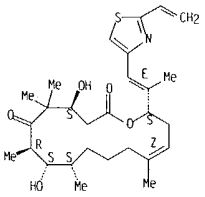
Absolute stereochemistry.
Double bond geometry as shown.



IT 204513-16-6P 204513-30-4P 240815-87-6P
252981-75-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilones and derivs. and their use against proliferative diseases)
RN 204513-16-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

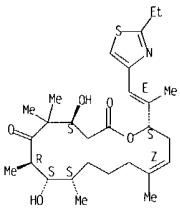
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 252981-45-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethyl-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

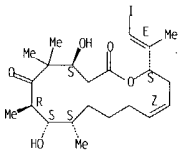
Absolute stereochemistry.
Double bond geometry as shown.



IT 252981-55-8 252981-56-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of epothilones and derivs. and their use against proliferative diseases)
RN 252981-55-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

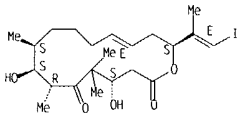
Absolute stereochemistry.

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



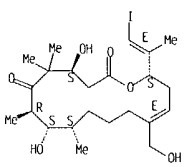
RN 204513-30-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 240815-87-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

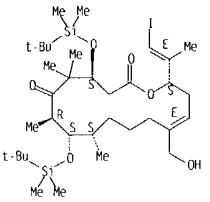
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 252981-75-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-

L5 ANSWER 73 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
dimethylethyl)dimethylsilyl]oxy]-13-(hydroxymethyl)-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-. (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 74 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:811249 CAPLUS
DOCUMENT NUMBER: 132:49105
TITLE: Epothilone minor constituents
INVENTOR(S): Hoefle, Gerhard; Reichenbach, Hans; Gerth, Klaus; Hardt, Ingo; Sasse, Florenz; Steinmetz, Heinrich
PATENT ASSIGNEE(S): Gesellschaft Fur Biotechnologische Forschung m.b.H. (Gbf), Germany
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965913	A2	19991223	WO 1999-EP4244	19990618 <--
WO 9965913	A3	20000420		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AU 9948995	A1	20000105	AU 1999-48995	19990618 <--
AU 757452	B2	20030220		
EP 1087975	A2	20010404	EP 1999-932700	19990618 <--
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AT 248174	E	20030915	AT 1999-932700	19990618
PT 1087975	T	20040130	PT 1999-932700	19990618
US 6624310	B1	20030923	US 2001-719932	20010321
US 2004049051	A1	20040311	US 2003-457098	20030606

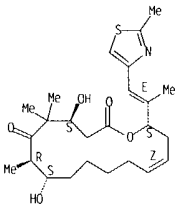
PRIORITY APPLN. INFO.: DE 1998-19826988 A 19980618
EP 1999-932700 A3 19990618
WO 1999-EP4244 W 19990618
US 2001-719932 A3 20010321

L5 ANSWER 74 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
ABSTRACT:
The invention relates to compds. which are obtained by fermenting DSM 6773, especially epothilones A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 and K and trans-epothilones C1 and C2.

IT **192370-82-4P**, Epothilone C4 **198475-12-6P**, Epothilone H1
198571-09-4P, Epothilone H2 **252917-44-5P**, Epothilone C7
252917-46-7P, Epothilone C8 **252917-47-8P**, Epothilone C9
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(epothilone minor constituents)

RN 192370-82-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

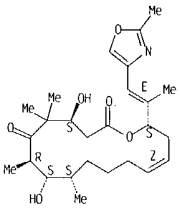
Absolute stereochemistry.
Double bond geometry as shown.



RN 198475-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

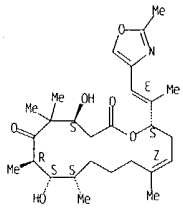
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 74 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-09-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

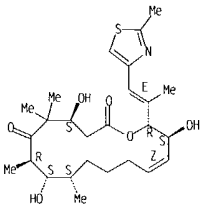
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 252917-44-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8,15-trihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,15S,16R)- (9CI) (CA INDEX NAME)

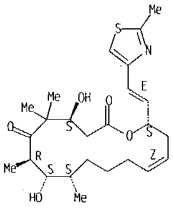
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 74 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 252917-46-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

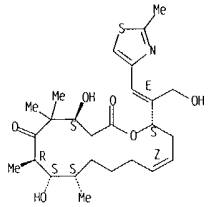
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 252917-47-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-1-(hydroxymethyl)-2-(2-methyl-4-thiazolyl)ethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

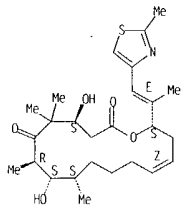
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 74 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 186692-73-9P, Epothilone C 189453-10-9P, Epothilone D
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(epothilone minor constituents)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

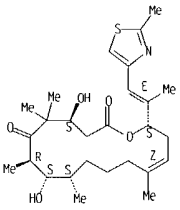
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-

L5 ANSWER 74 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

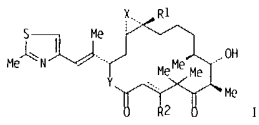


L5 ANSWER 75 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:691091 CAPLUS
DOCUMENT NUMBER: 131:310502
TITLE: synthesis and cytotoxicity of 12,13-modified epothilone derivatives for use in treatment of tumors or other hyperproliferative cellular disease
INVENTOR(S): Vite, Gregory D.; Kim, Soong-Hoon Kim; Hofle, Gerhard
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954319	A1	19991028	WO 1999-US7475	19990405 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG				
US 6380395	B1	20020430	US 1999-280192	19990329 .
US 6399638	B1	20020604	US 1999-280191	19990329
CA 2329181	AA	19991028	CA 1999-2329181	19990405 <--
AU 9934716	A1	19991108	AU 1999-34716	19990405 <--
AU 748526	B2	20020606		
BR 9909795	A	20001226	BR 1999-9795	19990405 <--
TR 200003036	T2	20010122	TR 2000-200003036	19990405 <--
EP 1073648	A1	20010207	EP 1999-916383	19990405 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002512239	T2	20020423	JP 2000-544658	19990405

PRIORITY APPLN. INFO.: US 1998-82564P P 19980421
WO 1999-US7475 W 19990405
OTHER SOURCE(S): MARPAT 131:310502
GRAPHIC IMAGE:

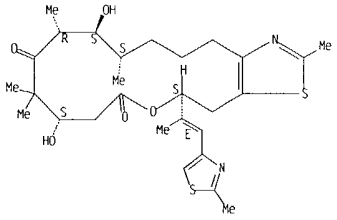


I

L5 ANSWER 75 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
ABSTRACT:
Synthesis and cytotoxicity of 12,13-modified epothilone derivs.(I) [R1 = H, (un)substituted alkyl; R2 = H if bond double or βOH if bond single; Y = O, NH; X = O, (un)substituted NH, OCH2, 2-methylthiazolo, S, (un)substituted CH2] is presented. Thus, I (R1 = H, X = NH, R2 = βOH, Y = O) (II) is prepared by epoxidn. of epothilone C followed by azidation and reductive imination. I are useful in treatment of tumors or other hyperproliferative cellular disease and show IC50 of 0.01-1000 nM in cell proliferation tests.

IT **247231-84-1P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and cytotoxicity of 12,13-modified epothilone derivs. for use in treatment of tumors or other hyperproliferative cellular disease)
RN 247231-84-1 CAPLUS
CN 5H-Oxacyclohexadecino[5,4-d]thiazole-7,11(4H,8H)-dione, 9,10,12,13,14,15,16,17-octahydro-9,13-dihydroxy-2,10,10,12,14-pentamethyl-5-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (5S,9S,12R,13S,14S)-(9CI) (CA INDEX NAME)

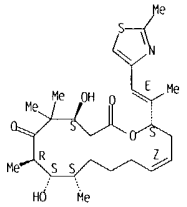
Absolute stereochemistry.
Double bond geometry as shown.



IT **186692-73-9**, Epothilone C
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and cytotoxicity of 12,13-modified epothilone derivs. for use in treatment of tumors or other hyperproliferative cellular disease)
RN 186692-73-9 CAPLUS

L5 ANSWER 75 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

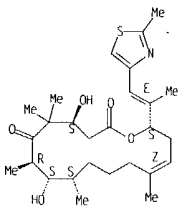
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **189453-10-9P**, Epothilone D **247230-54-2P**
247232-09-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and cytotoxicity of 12,13-modified epothilone derivs. for use in treatment of tumors or other hyperproliferative cellular disease)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

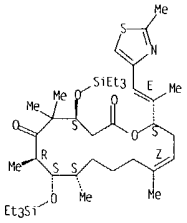
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 75 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 247230-54-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

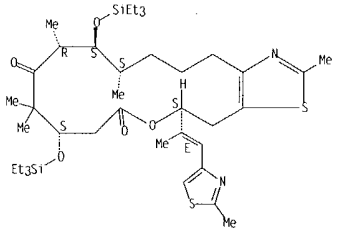
Absolute stereochemistry.
Double bond geometry as shown.



RN 247232-09-3 CAPLUS
CN 5H-Oxacyclohexadecino[5,4-d]thiazole-7,11(4H,8H)-dione, 9,10,12,13,14,15,16,17-octahydro-2,10,10,12,14-pentamethyl-5-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-9,13-bis[(triethylsilyl)oxy]-, (5S,9S,12R,13S,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 75 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

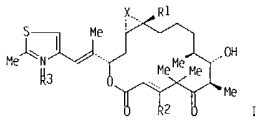
L5 ANSWER 76 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:691090 CAPLUS
DOCUMENT NUMBER: 131:310501
TITLE: synthesis and cytotoxicity of 12,13-cyclopropane epothilone derivatives for use in treatment of tumors or other hyperproliferative cellular disease
INVENTOR(S): Vite, Gregory D.; Kim, Soong-Hoon Kim; Höfle, Gerhard
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9954318	A1	19991028	WO 1999-US7448	19990405	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG					
US 6380395	B1	20020430	US 1999-280192	19990329	
US 6399638	B1	20020604	US 1999-280191	19990329	
CA 2323609	AA	19991028	CA 1999-2323609	19990405	<--
AU 9933827	A1	19991108	AU 1999-33827	19990405	<--
AU 757733	B2	20030306			
TR 200003036	T2	20010122	TR 2000-200003036	19990405	<--
EP 1073647	A1	20010207	EP 1999-915273	19990405	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002512238	T2	20020423	JP 2000-544657	19990405	

PRIORITY APPLN. INFO.: US 1998-82564P P 19980421
WO 1999-US7448 W 19990405
OTHER SOURCE(S): MARPAT 131:310501
GRAPHIC IMAGE:

L5 ANSWER 76 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

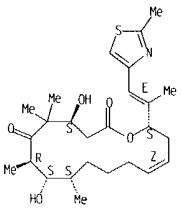
ABSTRACT:
Synthesis and cytotoxicity of 12,13-cyclopropane epothilone derivs. (I) [R1 = H, (un)substituted alkyl; R2 = H if bond double or βOH if bond single; R3 = electron pair or =O; X = (un)substituted CH2] is presented. Thus, I (R1 = Me, R2 = OH on single bond, R3 = electron pair, X = CH2) (II) is prepared by converting epothilone B to epothilone D via deepoxidn. followed by alc. protection, cyclopropanation and desilylation. I are useful in treatment of tumors or other hyperproliferative cellular disease and show IC50 values of 0.01-1000 nM in cell proliferation tests.

IT **186692-73-9P**, Epothilone C **186692-84-2P**
189453-10-9P, Epothilone d **247230-54-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and cytotoxicity of 12,13-cyclopropane epothilone derivs. for use in treatment of tumors or other hyperproliferative cellular disease)

RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

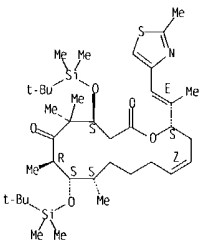
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 76 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

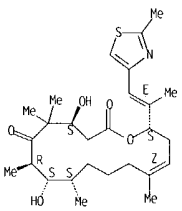
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

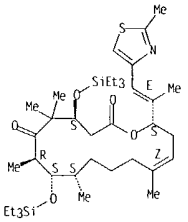
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 76 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 247230-54-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



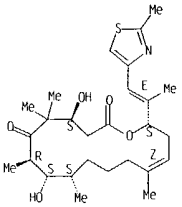
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 77 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:680932 CAPLUS
DOCUMENT NUMBER: 132:22767
TITLE: Complex Target-Oriented Synthesis in the Drug Discovery Process: A Case History in the dEpoB Series
AUTHOR(S): Harris, Christina R.; Danishefsky, Samuel J.
CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Journal of Organic Chemistry (1999), 64(23), 8434-8456
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with 103 refs. on complex target-oriented synthesis of naturally occurring cytotoxic agents of potential clin. value in the chemotherapy of cancer. In particular, the critical role of complex target-oriented synthesis in the discovery process pertinent to 12,13-desoxyepothilone B is described.

IT **189453-10-9P**, 12,13-Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(complex target-oriented synthesis in the drug discovery process of the desoxyepothilone B series)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 77 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 154 THERE ARE 154 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 78 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:663080 CAPLUS
DOCUMENT NUMBER: 132:22785
TITLE: Sets of Aldolase Antibodies with Antipodal Reactivities. Formal Synthesis of Epothilone E by Large-Scale Antibody-Catalyzed Resolution of Thiazole Aldol
AUTHOR(S): Sinha, Subhash C.; Sun, Jian; Miller, Gregory; Barbas, Carlos F. III; Lerner, Richard A.
CORPORATE SOURCE: Department of Molecular Biology and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Organic Letters (1999), 1(10), 1623-1626
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:22785
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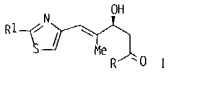
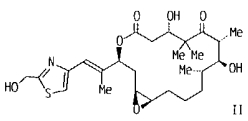


I

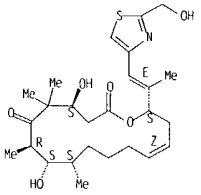


II

ABSTRACT:
Three monoclonal aldolase antibodies, generated against a β-diketone hapten by reactive immunization, catalyzed rapid and highly enantioselective retro-aldol reactions of ent-I (R = R1 = Me; R = Et, Pr, Bu, 1-pentyl, 1-butenyl, CH2F, R1 = Me; R = Me, R1 = CH2OH, OMe, SMe; R = Et, R1 = SMe), providing optically pure I by kinetic resolution. Compds. (±)-I (R = R1 = Me; R = Me, R1 = CH2OH; R = Et, R1 = SMe) have been resolved in multigram quantities using 0.003, 0.005, and 0.0004 mol % antibody catalysts, resp. Resolved compds. I are useful synthons for the construction of epothilones A-E and their analogs. Here, a formal synthesis of epothilone E (II), has been achieved starting from compound I (R = Me, R1 = CH2OH).

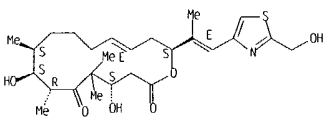
IT **204513-12-2P** **204513-14-4P**
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(formal synthesis of epothilone E by large-scale antibody-catalyzed resoln. of thiazole aldol)
RN 204513-12-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



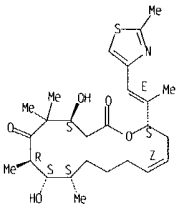
RN 204513-14-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



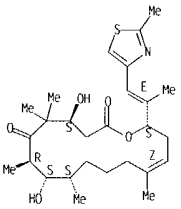
IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: PNU (Preparation, unclassified); PREP (Preparation)
(formal synthesis of epothilone E by large-scale antibody-catalyzed resolution of thiazole aldol)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

L5 ANSWER 78 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

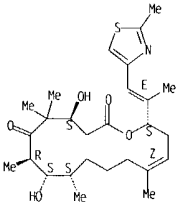
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

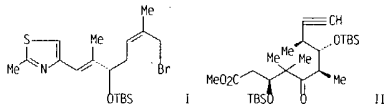
L5 ANSWER 79 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
assembly of subunits)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

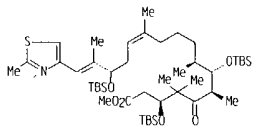
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 79 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:643350 CAPLUS
DOCUMENT NUMBER: 132:3269
TITLE: Improved Synthesis of Epothilone B Employing Alkylation of an Alkyne for Assembly of Subunits
AUTHOR(S): White, James D.; Sundermann, Kurt F.; Carter, Rich G.
CORPORATE SOURCE: Department of Chemistry, Oregon State University, Corvallis, OR, 97331-4003, USA
SOURCE: Organic Letters (1999), 1(9), 1431-1434
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:3269
GRAPHIC IMAGE:

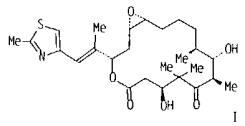


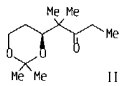


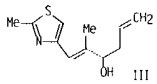
ABSTRACT:
A strategy for assembling the two principal modules of epothilone B was developed that merges allylic bromide (I) with a terminal acetylene (II) to fabricate the C10-C11 bond of the macrocycle. The resulting alkyne was semihydrogenated to give a seco ester (III) previously employed in our total synthesis of epothilone B. This new approach affords a more efficient route to the naturally occurring macrolide and to its 9,10-dehydro analog.

IT 189453-10-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of epothilone B employing alkylation of an alkyne for

L5 ANSWER 80 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:606635 CAPLUS
DOCUMENT NUMBER: 131:351124
TITLE: Total synthesis of (-)-epothilone A
AUTHOR(S): Schinzer, Dieter; Bauer, Armin; Bohm, Oliver M.; Limberg, Anja; Cordes, Martin
CORPORATE SOURCE: Chemisches Institut der Otto-von-Guericke-Universitat, Magdeburg, D-39106, Germany
SOURCE: Chemistry--A European Journal (1999), 5(9), 2483-2491
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:351124
GRAPHIC IMAGE:





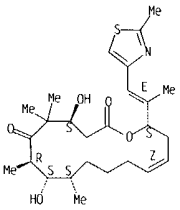


ABSTRACT:
The total synthesis of (-)-epothilone A (I) by a convergent route is reported. The synthesis of the required key intermediates has been improved with respect to stereoselectivity and availability. The access to Et ketone II has been significantly improved by employment of chiral acetate equivalent, which provided higher optical and chemical yields. Key intermediate (S)-H2C:CH(CH2)3CHMeCHO was obtained by oxazolidinone auxiliary techniques and stereoselectively coupled with II by an aldol reaction. After esterification with thiazole fragment III, (-)-epothilone A (I) was finally constructed by using ring-closing metathesis.

IT 186692-73-9P, Epothilone C 186692-84-2P, Epothilone C bis(tert-butyldimethylsilyl) ether 188260-10-8P
188260-22-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(convergent stereoselective total synthesis of (-)-epothilone A)

L5 ANSWER 80 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

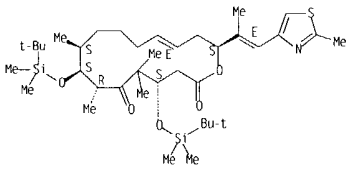
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

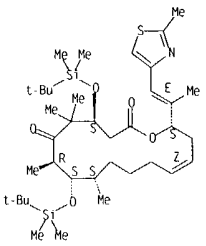
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 80 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



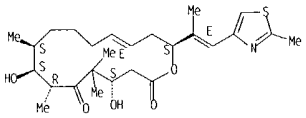
REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 80 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-22-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 81 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1999:589150 CAPLUS
DOCUMENT NUMBER:	131:336853
TITLE:	The synthesis and evaluation of 12,13-benzodesoxyepothilone B: a highly convergent route
AUTHOR(S):	Glunz, Peter W.; He, Lifeng; Horwitz, Susan B.; Chakravarty, Subrata; Ojima, Iwao; Chou, Ting-Chao; Danishefsky, Samuel J.
CORPORATE SOURCE:	Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE:	Tetrahedron Letters (1999), 40(38), 6895-6898 CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER:	Elsevier Science Ltd.
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 131:336853
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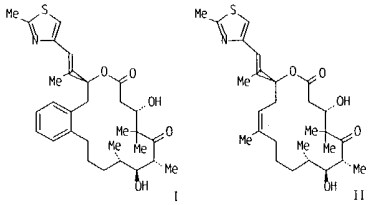


I II

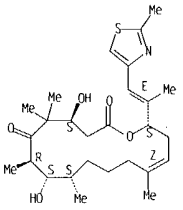
ABSTRACT:
The title compound I retains some of the affinity for microtubule assemblies as does 12,13-desoxyepothilone B (II).

IT **189453-10-9DP**, 12,13-Desoxyepothilone B, analog
246529-73-7P, 12,13-Benzodeoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and affinity for microtubule assembly of 12,13-benzodesoxyepothilone B)

RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-

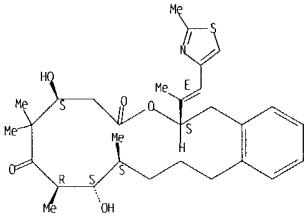
L5 ANSWER 81 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



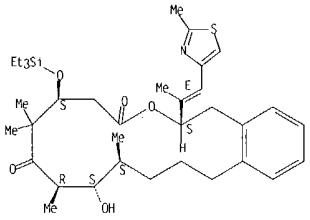
RN 246529-73-7 CAPLUS
CN 2H-3-Benzoxacyclohexadecin-4,8(5H,9H)-dione, 1,6,7,10,11,12,13,14-octahydro-6,10-dihydroxy-7,7,9,11-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (2S,6S,9R,10S,11S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 246530-13-2P 246530-14-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and affinity for microtubule assembly of

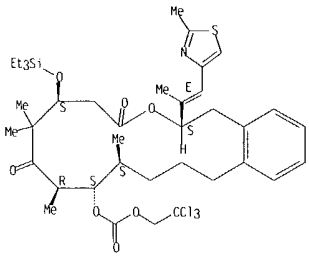
L5 ANSWER 81 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 81 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
12,13-benzodesoxyepothilone B)
RN 246530-13-2 CAPLUS
CN Carbonic acid, (2S,6S,9R,10S,11S)-1,4,5,6,7,8,9,10,11,12,13,14-dodecahydro-7,7,9,11-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-dioxo-6-[(triethylsilyl)oxy]-2H-3-benzoxacyclohexadecin-10-yl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 246530-14-3 CAPLUS
CN 2H-3-Benzoxacyclohexadecin-4,8(5H,9H)-dione, 1,6,7,10,11,12,13,14-octahydro-10-hydroxy-7,7,9,11-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-6-[(triethylsilyl)oxy]-, (2S,6S,9R,10S,11S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1999:566025 CAPLUS
DOCUMENT NUMBER:	131:199557
TITLE:	Synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype
INVENTOR(S):	Danishefsky, Samuel J.; Balog, Aaron; Bertinato, Peter; Su, Dai-Shi; Chou, Ting-Chau; Meng, Dongfang; Kamenecka, Ted; Sorensen, Erik J.; Kuduk, Scott; Harris, Christina; Zhang, Xiu-Guo; Bertino, Joseph R.
PATENT ASSIGNEE(S):	Sloan-Kettering Institute for Cancer Research, USA
SOURCE:	PCT Int. Appl., 264 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	4
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943653	A1	19990902	WO 1999-US4008	19990224 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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CA 2322157	AA	19990902	CA 1999-2322157	19990224 <--
AU 9927858	A1	19990915	AU 1999-27858	19990224 <--
AU 758526	B2	20030320		
EP 1058679	A1	20001213	EP 1999-908420	19990224 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002504540	T2	20020212	JP 2000-533411	19990224
NZ 506742	A	20030926	NZ 1999-506742	19990224

PRIORITY APPLN. INFO.:	US 1998-75947P	P	19980225
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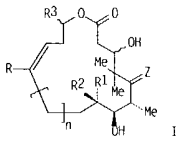
	US 1998-97733P	P	19980824
	WO 1999-US4008	W	19990224

OTHER SOURCE(S):	MARPAT 131:199557
GRAPHIC IMAGE:	

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

ABSTRACT:
Syntheses of epothilone A and B, desoxyepothilones A and B, and analogs (I) [R,R1,R2 = independently H, (un)substituted linear or branched chain alkyl; R3 = CHY=CHX, H, linear or branched chain alkyl, Ph, 2-methyl-1,3-thiazolinyl, 2-, 3-, or 4-furanyl, 2-, 3-, or 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3- or 6-indolyl; X = H, linear or branched chain alkyl, Ph, 2-methyl-1,3-thiazolinyl, 2-, 3-, or 4-furanyl, 2-, 3-, or 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3- or 6-indolyl; Y = H, linear or branched chain alkyl; Z = O, substituted NOH, substituted NNH2; n = 1-2] and their intermediates are described. Activities of novel compns. based on I and methods for the treatment of cancer and cancer which has developed a multidrug-resistant phenotype are presented.

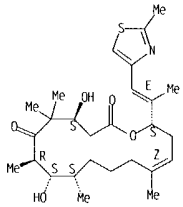
IT **189453-10-9P**, Desoxyepothilone B **198475-05-7P**
219824-14-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)

RN 189453-10-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

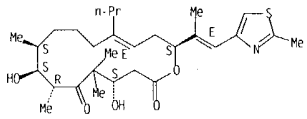
L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-05-7 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

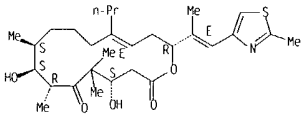


RN 219824-14-3 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

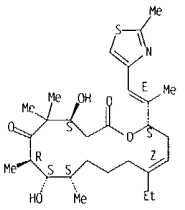


IT **198475-04-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)

RN 198475-04-6 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



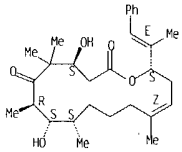
IT **198475-13-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)

RN 198475-13-7 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

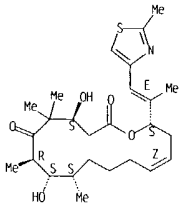


IT **186692-73-9**, Desoxyepothilone A **188259-95-2**
188260-10-8 **189453-40-5** **192370-82-4**
198475-06-8 **198475-07-9** **198475-11-5**
198475-12-6 **219824-38-1** **241129-05-5**
241129-07-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)

RN 186692-73-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

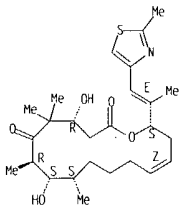


RN 188259-95-2 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

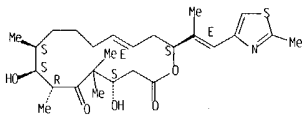
Absolute stereochemistry. Rotation (-).

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

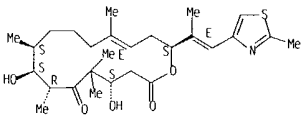
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

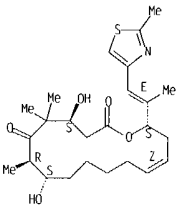
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 192370-82-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

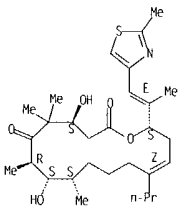
Absolute stereochemistry.
Double bond geometry as shown.



RN 198475-06-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

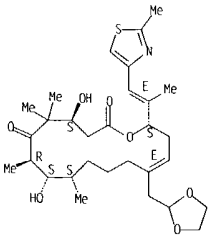
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-07-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(1,3-dioxolan-2-ylmethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

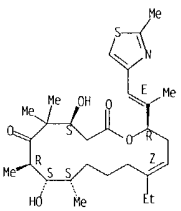
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198475-11-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16R)- (9CI) (CA INDEX NAME)

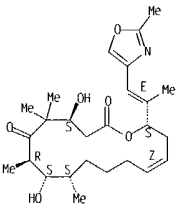
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

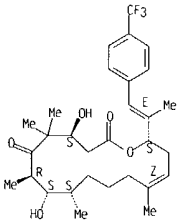
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 219824-38-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-[4-(trifluoromethyl)phenyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

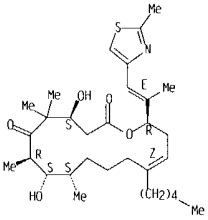
L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 241129-05-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-pentyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

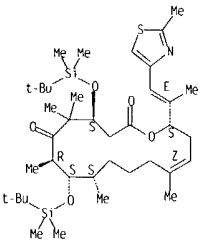
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 241129-07-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-pentyl-, (4S,7R,8S,9S,13Z,16R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



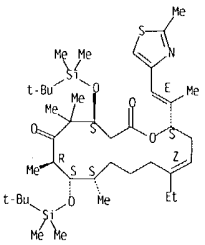
IT **186692-84-2P 189453-35-8P 209261-05-2P**
219824-09-6P 219824-13-2P 219824-19-8P

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 209261-05-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-ethyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

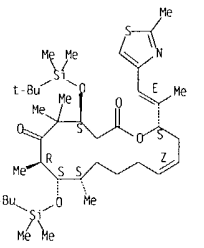


RN 219824-09-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
219824-25-6P 219824-29-0P 241129-40-8P
241129-41-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)
RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

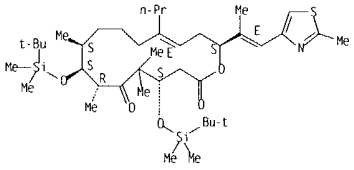
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

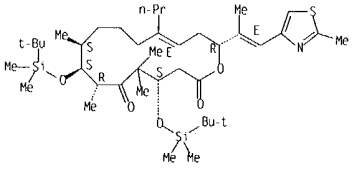
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 219824-13-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16R)- (9CI) (CA INDEX NAME)

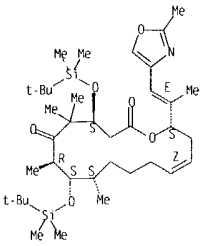
Absolute stereochemistry.
Double bond geometry as shown.



RN 219824-19-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

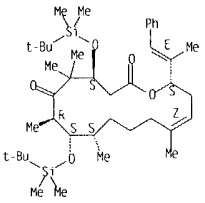
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 219824-25-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

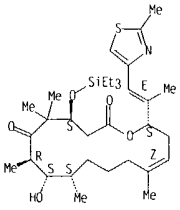


RN 219824-29-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(1,3-dioxolan-2-ylmethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

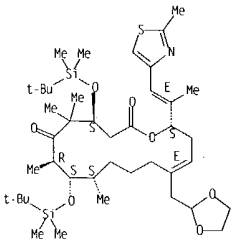
L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



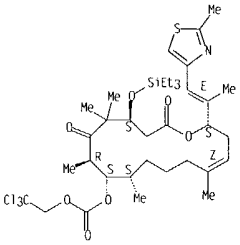
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 82 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 241129-40-8 CAPLUS
CN Carbonic acid, (4S,7R,8S,9S,13Z,16S)-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-2,6-dioxo-4-[(triethylsilyl)oxy]oxacyclohexadec-13-en-8-yl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



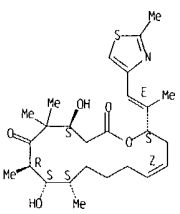
RN 241129-41-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-5,5,7,9,13-pentamethyl-16-

L5 ANSWER 83 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:470234 CAPLUS
DOCUMENT NUMBER: 131:286303
TITLE: N-oxidation of epothilone A-C and O-acyl rearrangement to C-19- and C-21-substituted epothilones
AUTHOR(S): Hofle, Gerhard; Glaser, Nicole; Kiffe, Michael; Hecht, Hans-Jurgen; Sasse, Florenz; Reichenbach, Hans
CORPORATE SOURCE: Abteilung Naturstoffchemie Gesellschaft fur Biotechnologische Forschung, Braunschweig, D-38124, Germany
SOURCE: Angewandte Chemie, International Edition (1999), 38(13/14), 1971-1974
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:286303
ABSTRACT:
Epothilones A-C underwent N-oxidation on treatment with MCPBA in CH2Cl2. The N-oxide of epothilones A and B were converted to the 2-acetoxymethylthiazole derivs. with Ac2O and these were hydrolyzed to epothilones E and F. Some chloro and tosyloxy derivs. were also prepared. In vitro antitumor activities are reported.

IT **186692-73-9**, Epothilone C **189453-10-9**, Epothilone D
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(N-oxidation of epothilone A-C, O-acyl rearrangement and antitumor activity)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

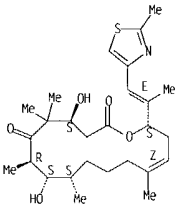
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 83 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

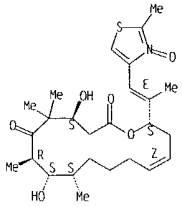
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT 246520-37-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(N-oxidation of epothilone A-C, O-acyl rearrangement and antitumor activity)
RN 246520-37-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-3-oxido-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 83 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 84 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

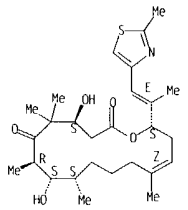
ACCESSION NUMBER:	1999:444724 CAPLUS
DOCUMENT NUMBER:	131:286299
TITLE:	New Chemical Synthesis of the Promising Cancer Chemotherapeutic Agent 12,13-Desoxyepothilone B: Discovery of a Surprising Long-Range Effect on the Diastereoselectivity of an Aldol Condensation
AUTHOR(S):	Harris, Christina R.; Kuduk, Scott D.; Balog, Aaron; Savin, Ken; Glunz, Peter W.; Danishefsky, Samuel J.
CORPORATE SOURCE:	Laboratory for Bioorganic Chemistry, The Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE:	Journal of the American Chemical Society (1999), 121(30), 7050-7062 CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 131:286299
GRAPHIC IMAGE:	

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
The epothilones are naturally occurring cytotoxic mols. that possess the remarkable ability to arrest cell division through the stabilization of microtubule assemblies. In vivo studies with 12,13-desoxyepothilone B (dEpoB) (I), have established that the desoxy compound is well tolerated and virtually curative against a variety of sensitive and resistant xenograft tumors in animal models. In light of these discoveries, a chemical synthesis of dEpoB would be able to support a serious and substantial discovery research program directed toward the clin. development of this mol. The overall strategy for this endeavor assumed the ability to synthesize dEpoB from three constructs which include an achiral β,δ-diketo ester construct A (II), an (S)-2-methylpentenal moiety B (III), and the thiazoyl-containing vinyl iodide moiety C (IV). It was envisioned that a diastereoselective aldol condensation between an achiral C5-C6 (Z)-metalloenolate derived from construct A and an (S)-2-methylalkanal fragment, B, would generate the desired C6-C7 bond. Second, a B-alkyl Suzuki coupling between the vinyl iodide construct C and an alkyl borane would form the C11-C12 bond. Finally, a late-stage reduction of the C3 ketone to the requisite C3 alc. with high asym. induction would permit introduction of the β,δ-diketo ester fragment A, into the synthesis as a readily accessible achiral building block. The governing concepts the new synthesis are described.

IT 189453-10-9P, 12,13-Deoxyepothilone B 241129-40-8P
241129-41-9P 246529-73-7P 246530-13-2P
246530-14-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of promising cancer chemotherapeutic agent 12,13-desoxyepothilone B, discovery of a surprising long-range effect on diastereoselectivity of aldol condensation)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

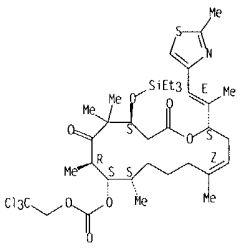
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 241129-40-8 CAPLUS
CN Carbonic acid, (4S,7R,8S,9S,13Z,16S)-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-2,6-dioxo-4-[(triethylsilyl)oxy]oxacyclohexadec-13-en-8-yl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

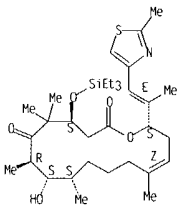
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 84 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 241129-41-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 8-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

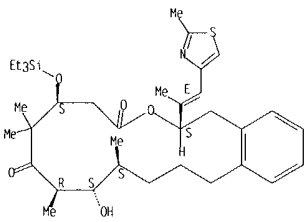


RN 246529-73-7 CAPLUS
CN 2H-3-Benzoxacyclohexadecin-4,8(5H,9H)-dione, 1,6,7,10,11,12,13,14-octahydro-6,10-dihydroxy-7,7,9,11-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (2S,6S,9R,10S,11S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

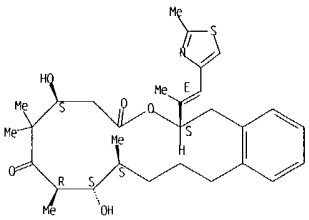
L5 ANSWER 84 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



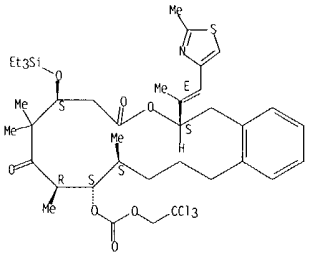
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 84 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 246530-13-2 CAPLUS
CN Carbonic acid, (2S,6S,9R,10S,11S)-1,4,5,6,7,8,9,10,11,12,13,14-dodecahydro-7,7,9,11-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-dioxo-6-[(triethylsilyl)oxy]-2H-3-benzoxacyclohexadecin-10-yl 2,2,2-trichloroethyl ester (9CI) (CA INDEX NAME)

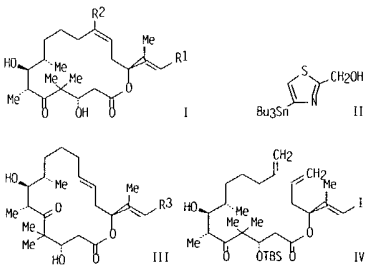
Absolute stereochemistry.
Double bond geometry as shown.



RN 246530-14-3 CAPLUS
CN 2H-3-Benzoxacyclohexadecin-4,8(5H,9H)-dione, 1,6,7,10,11,12,13,14-octahydro-10-hydroxy-7,7,9,11-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-6-[(triethylsilyl)oxy]-, (2S,6S,9R,10S,11S)- (9CI) (CA

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1999:383492 CAPLUS
DOCUMENT NUMBER:	131:199535
TITLE:	Total synthesis of epothilone E and related side-chain modified analogues via a Stille coupling based strategy
AUTHOR(S):	Nicolaou, K. C.; King, N. P.; Finlay, M. R. V.; He, Y.; Roschangar, F.; Vourloumis, D.; Vallberg, H.; Sarabia, F.; Ninkovic, S.; Hepworth, D.
CORPORATE SOURCE:	Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE:	Bioorganic & Medicinal Chemistry (1999), 7(5), 665-697 CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER:	Elsevier Science Ltd.
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 131:199535
GRAPHIC IMAGE:	



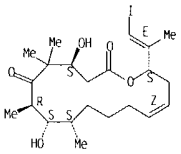
ABSTRACT:
A Stille coupling strategy has been utilized to complete a total synthesis of epothilone E from vinyl iodide I (R1 = I; R2 = H) and thiazolestannane II. The central core fragment I (R1 = I; R2 = H) and its trans-isomer III (R3 = I) were prepared from triene IV (TBS = SiMe2CMe3) using ring-closing metathesis (RCM), and were subsequently coupled to a variety of alternative stannanes to provide a library of epothilone analogs I [R1 = 2-(5-acetoxypentyl)thiazol-4-yl, 2-(methylthio)thiazol-4-yl, 2-piperidinothiazol-4-yl, 2-methoxythiazol-4-yl, 2-ethoxythiazol-4-yl, thiazol-4-yl, thiazol-2-yl, thiazol-5-yl,

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
2-(hydroxymethyl)thiazol-4-yl, 2-(acetoxymethyl)thiazol-4-yl, 2-(fluoromethyl)thiazol-4-yl, 2-vinylthiazol-4-yl, 2-ethylthiazol-4-yl, 2-furyl, 2-thienyl, Ph, 3-pyridyl, CH:C(OEt)Me-(Z), R2 = HJ and III [R3 = 2-(5-acetoxypentyl)thiazol-4-yl, 2-(methylthio)thiazol-4-yl, 2-piperidinothiazol-4-yl, 2-methoxythiazol-4-yl, 2-ethoxythiazol-4-yl, thiazol-4-yl, thiazol-2-yl, thiazol-5-yl, 2-(hydroxymethyl)thiazol-4-yl, 2-(acetoxymethyl)thiazol-4-yl, 2-(fluoromethyl)thiazol-4-yl, 2-vinylthiazol-4-yl, 2-ethylthiazol-4-yl, 2-furyl, 2-thienyl, Ph, 3-pyridyl, CH:C(OEt)Me-(Z)]. The Stille coupling approach was then used to prep. epothilone B analogs from the key macrolactone intermediate I (R1 = I, R2 = CH2OH) which was itself synthesized by a macrolactonization based strategy.

IT **204513-16-6P 204513-26-8P 204513-28-0P**
204513-30-4P 240816-03-9P 240816-04-0P
240816-05-1P 240816-06-2P 240816-08-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of epothilone E and related side-chain modified analogs via a Stille coupling based strategy)

RN 204513-16-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

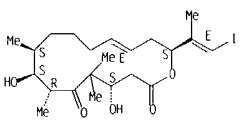
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 204513-26-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

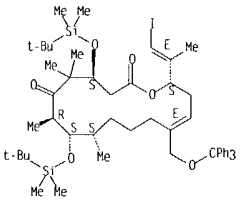
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-03-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-13-[(triphenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

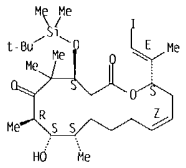
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-04-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

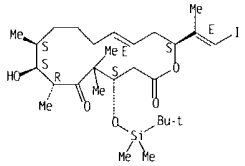
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-28-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

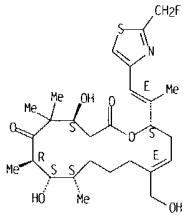
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-30-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

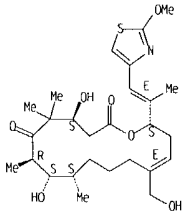
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-05-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-16-[(1E)-2-(2-methoxy-4-thiazolyl)-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

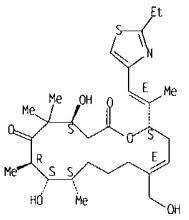
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-06-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethyl-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

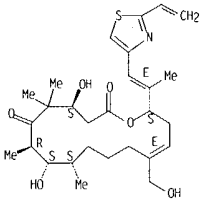
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-08-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethenyl-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

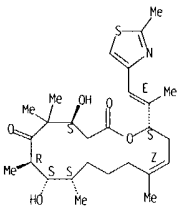


IT **186692-73-9DP**, Epothilone C, analogs **188260-10-8DP**, trans-Epothilone C, analogs **189453-10-9DP**, Epothilone D, analogs
204513-12-2P 204513-14-4P 204513-35-9P
204513-36-0P 204513-37-1P 204513-38-2P
204513-39-3P 204513-40-6P 204513-41-7P
204513-42-8P 204513-43-9P 204513-44-0P
204513-45-1P 204513-46-2P 204513-47-3P
204513-48-4P 204513-49-5P 204513-50-8P
204513-51-9P 204513-52-0P 204513-53-1P

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

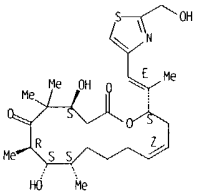
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 204513-12-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

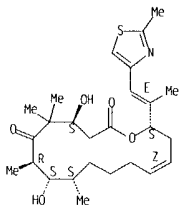
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 204513-14-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

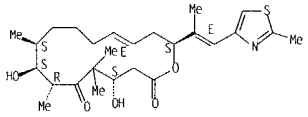
L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
204513-54-2P 209260-90-2P 209260-91-3P
209260-96-8P 209260-97-9P 240815-87-6P
240816-07-3P 240816-09-5P 240816-10-8P
240816-11-9P 240816-12-0P 240816-36-8P
240816-37-9P 240816-38-0P 240816-39-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of epothilone E and related side-chain modified analogs via a Stille coupling based strategy)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

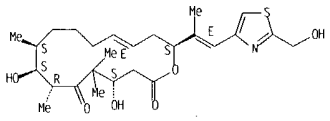


RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

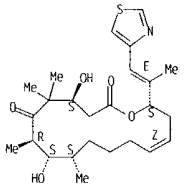


L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

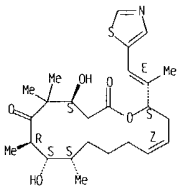
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-36-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

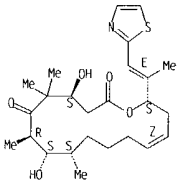
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-37-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

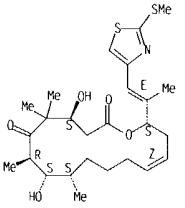
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-38-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[5-(acetyloxy)pentyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

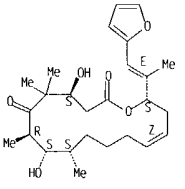
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-41-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

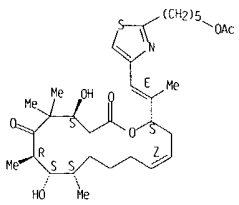
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-42-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

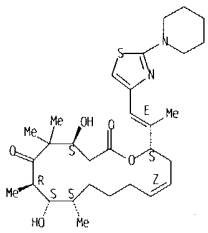
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-39-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(1-piperidinyl)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

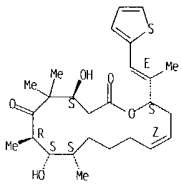
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-40-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

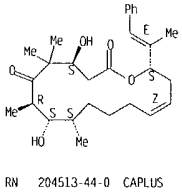
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-43-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

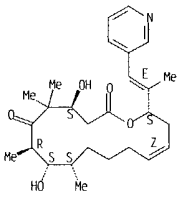
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-44-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

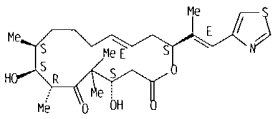
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-45-1 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

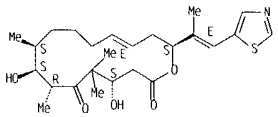
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-46-2 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

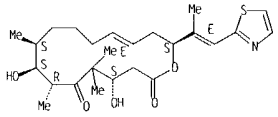
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



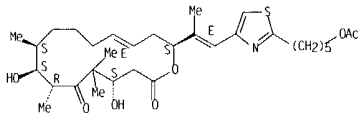
RN 204513-47-3 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(2-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-48-4 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 16-[(1E)-2-[2-[5-(acetyloxy)pentyl]-4-thiazolyl]-1-methylethenyl]-4.8-dihydroxy-5.5.7.9-tetramethyl-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

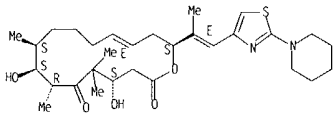
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-49-5 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-[2-(1-piperidinyl)-4-thiazolyl]ethenyl]-.

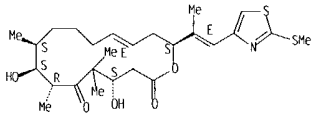
L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



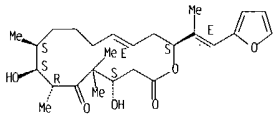
RN 204513-50-8 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-51-9 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4.8-dihydroxy-5.5.7.9-tetramethyl-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

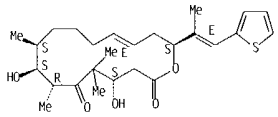
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-52-0 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA

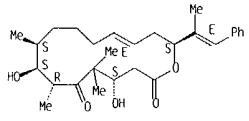
L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



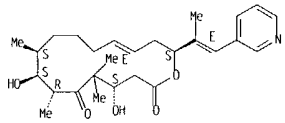
RN 204513-53-1 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-54-2 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

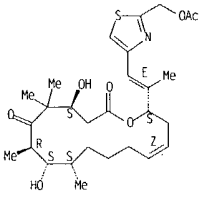
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-90-2 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 16-[(1E)-2-[2-[(acetyloxy)methyl]-4-thiazolyl]-1-methylethenyl]-4.8-dihydroxy-5.5.7.9-tetramethyl-.

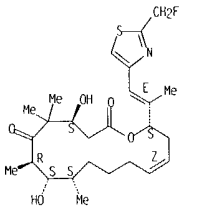
L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-91-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

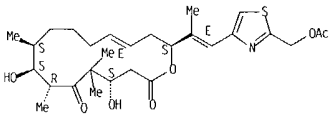
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-96-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[(acetyloxy)methyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

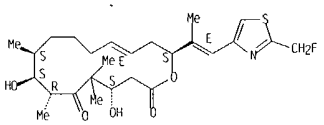
Absolute stereochemistry.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



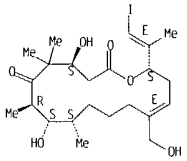
RN 209260-97-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 240815-87-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

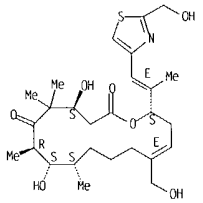
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

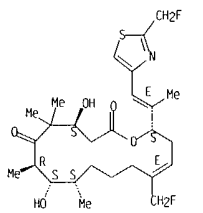
RN 240816-07-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-09-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(fluoromethyl)-16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

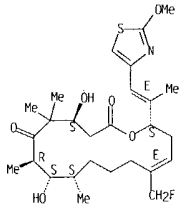
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(fluoromethyl)-4,8-dihydroxy-16-[(1E)-2-(2-methoxy-4-thiazolyl)-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

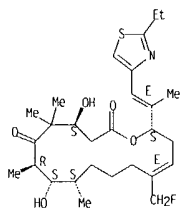
Absolute stereochemistry. Rotation (-).

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 240816-11-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethyl-4-thiazolyl)-1-methylethenyl]-13-(fluoromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

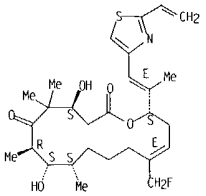
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-12-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethenyl-4-thiazolyl)-1-methylethenyl]-13-(fluoromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

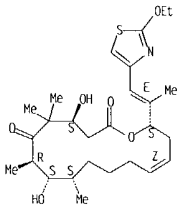
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 240816-36-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethoxy-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

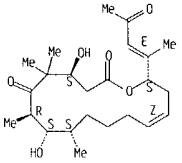


RN 240816-37-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-3-oxo-1-butenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

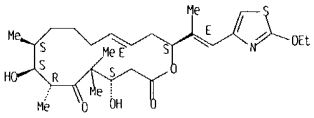
L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 85 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



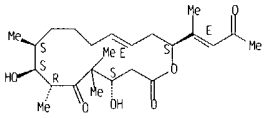
RN 240816-38-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethoxy-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 240816-39-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-3-oxo-1-butenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

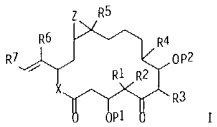


L5 ANSWER 86 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:375551 CAPLUS
DOCUMENT NUMBER: 131:31830
TITLE: A process for the reduction of oxiranyl epothilones to olefinic epothilones
INVENTOR(S): Kim, Soong-Hoon; Johnson, James A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

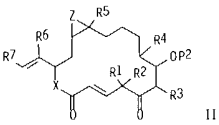
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9928324	A1	19990610	WO 1998-US25464	19981201 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2311929	AA	19990610	CA 1998-2311929	19981201 <--
AU 9915408	A1	19990616	AU 1999-15408	19981201 <--
AU 738576	B2	20010920		
EP 1042327	A1	20001011	EP 1998-959652	19981201 <--
EP 1042327	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001525324	T2	20011211	JP 2000-523216	19981201 <--
AT 250066	E	20031015	AT 1998-959652	19981201

PRIORITY APPLN. INFO.: US 1997-67549P P 19971204
US 1998-82563P P 19980421
WO 1998-US25464 W 19981201
OTHER SOURCE(S): CASREACT 131:31830; MARPAT 131:31830
GRAPHIC IMAGE:

L5 ANSWER 86 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I



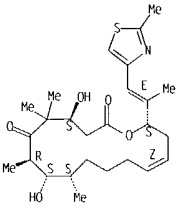
II

ABSTRACT:
The olefinic epothilones I and II (X = O, NR8; Z = bond; R1-R6 = H, alkyl, substituted alkyl, aryl; R1R2 may be a cycloalkyl; R7 = H, alkyl, substituted alkyl, aryl, cycloalkyl, heterocyclo; R8 = H, alkyl, substituted alkyl, OH, alkoxy, substituted alkoxy; P1, P2 = H, alkyl, substituted alkyl, alkanoyl, substituted alkanoyl, aroyl, substituted aroyl, trialkylsilyl, aryldialkylsilyl, diarylalkylsilyl, triarylsilyl) were prepared by reduction of the oxiranyl epothilones I and II (Z = O) with a metal or metal assisted reagents, e.g. metallocenes, WCl4-BuLi, VCl3-Zn, TiCl3-LiAlH4. Thus, epothilone A was treated with Mg and bis(cyclopentadienyl)titanium dichloride in THF to give 80% epothilone C.

IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
226956-19-0P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for reduction of oxiranyl epothilones to olefinic epothilones)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

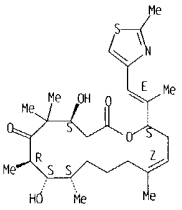
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 86 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

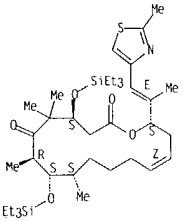
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 226956-19-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 86 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 87 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

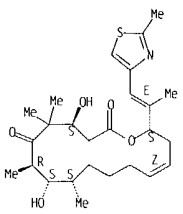
ACCESSION NUMBER: 1999:322978 CAPLUS
DOCUMENT NUMBER: 131:124926
TITLE: A Unified and Quantitative Receptor Model for the Microtubule Binding of Paclitaxel and Epothilone
AUTHOR(S): Wang, Minmin; Xia, Xiaoyang; Kim, Yohan; Hwang, David; Jansen, Johanna M.; Botta, Maurizio; Liotta, Dennis C.; Snyder, James P.
CORPORATE SOURCE: Department of Chemistry, Emory University, Atlanta, GA, 30322, USA
SOURCE: Organic Letters (1999), 1(1), 43-46
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

ABSTRACT:
Paclitaxel and epothilone represent the two major classes of antimicrotubule agents that promote tubulin polymerization and, presumably, mitotic arrest during cell division. A common minireceptor binding site model at β-tubulin has been constructed for these structurally divergent compds. Utilizing 20 amino acids identified in photoaffinity labeling expts., the 3-D model correlates measured and predicted Ki's with r = 0.99 and rms(ΔGcalc - ΔGexp) = 0.2 kcal/mol. In addition, the model predicts the affinity of compds. not used in the training set and explains much of the SAR for the paclitaxel and epothilone families.

IT **186692-73-9**, Desoxyepothilone A **189453-10-9**, Desoxyepothilone B **189453-40-5** **193146-35-9**
220773-73-9
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(A Unified and Quant. Receptor Model for the Microtubule Binding of Paclitaxel and Epothilone)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

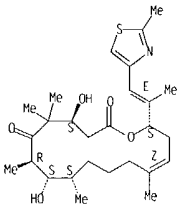
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 87 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

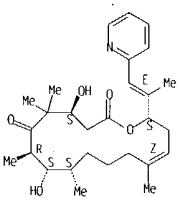
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

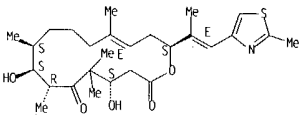
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 87 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



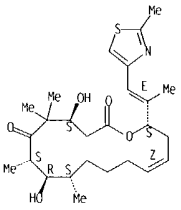
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 87 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 193146-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 220773-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

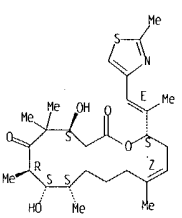
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 88 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:183183 CAPLUS
DOCUMENT NUMBER: 130:337931
TITLE: Dianion equivalents corresponding to the polypropionate domain of epothilone B
AUTHOR(S): Harris, Christina R.; Kuduk, Scott D.; Savin, Ken; Balog, Aaron; Danishefsky, Samuel J.
CORPORATE SOURCE: Laboratory Bioorganic Chemistry, Sloan-Kettering Institute Cancer Research, New York, NY, 10021, USA
SOURCE: Tetrahedron Letters (1999), 40(12), 2263-2266
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:337931
ABSTRACT:
A modified synthesis of the polypropionate portion of epothilone, which utilizes a novel, diastereoselective aldol reaction of (S)-2-methyl-4-pentenal and the Z-enolate of the tricarbonyl species EtCOCMe2COCH2CO2CMe3 is reported.

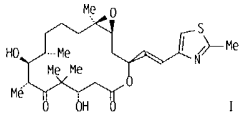
IT **189453-10-9P**, Desoxyepothilone B
RL: PNU (Preparation, unclassified); PREP (Preparation)
(dianion equivalent corresponding to the polypropionate domain of epothilone B)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 89 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:176999 CAPLUS
DOCUMENT NUMBER: 131:31819
TITLE: Synthesis of 16-desmethylepothilone B: improved methodology for the rapid, highly selective and convergent construction of epothilone Bepothilone B and analogs
AUTHOR(S): Nicolaou, K. C.; Hepworth, David; Finlay, M. Ray V.; Paul King, N.; Werschkun, Barbara; Bigot, Antony
CORPORATE SOURCE: Department of Chemistry, The Skaggs Inst. Chem. Biol., The Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: Chemical Communications (Cambridge) (1999), (6), 519-520
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:31819
GRAPHIC IMAGE:



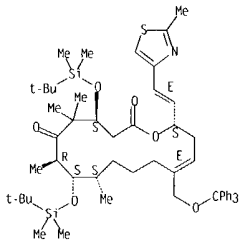
I

ABSTRACT:
During a synthesis of 16-desmethylepothilone B (I) new methods for the convergent and highly stereoselective synthesis of epothilone B and analogs were developed.

IT **226940-49-4 226940-50-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective synthesis of 16-desmethylepothilone B and precursors of epothilone B and analogs)
RN 226940-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-13-[(triphenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

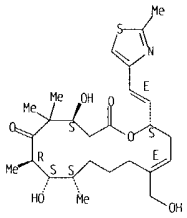
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 89 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 226940-50-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



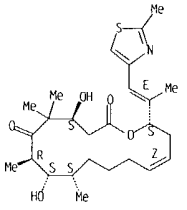
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 90 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:145094 CAPLUS
DOCUMENT NUMBER: 131:13461
TITLE: The microtubule-stabilizing agents epothilones A and B and their desoxy-derivatives induce mitotic arrest and apoptosis in human prostate cancer cells
AUTHOR(S): Sepp-Lorenzino, L.; Balog, A.; Su, D.-S.; Meng, D.; Timaul, N.; Scher, H. I.; Danishefsky, S. J.; Rosen, N.
CORPORATE SOURCE: Program in Cell Biology, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Prostate Cancer and Prostatic Diseases (1999), 2(1), 41-52
CODEN: PCPDFW; ISSN: 1365-7852
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Epothilones are a new class of natural products that bind to tubulin and prevent the depolymn. of microtubules, although they have no structural similarity to paclitaxel. Taxanes are only marginally effective in the treatment of disseminated prostate cancer, although they may have useful activity when administered in combination with estramustine. Unlike paclitaxel, epothilones are not substrates for P-glycoprotein and are active in multidrug resistant cells. Epothilones A and B (EA, EB) have recently been synthesized in toto. In this report, we examine the effects of synthetic epothilones and their desoxy derivs., as well as paclitaxel, on prostate cancer cell lines. EB was the most active of these compds. in tissue culture (IC50:50-75pM), four to ten-fold more potent than paclitaxel. EA and the desoxyderivatives of EA and EB (dEA, dEB) were also active, but less potent than EB. Each of these compds. causes mitotic block followed by apoptotic cell death. The relative potencies for cell cycle arrest and cytotoxicity directly correlate with the ability of the drugs to bind microtubules, stabilize mitotic spindles and induce the formation of interphase microtubule bundles. Therefore, synthetic epothilones are potent inhibitors of prostate cancer cell lines and work in a fashion similar to paclitaxel. Recently, we showed that farnesyl transferase inhibitors sensitize tumor cells to paclitaxel-induced mitotic arrest. We now have extended these observations to show that paclitaxel and the epothilones synergize with FTI to arrest the growth of prostate cancer cells. Moreover, this occurs in DU145, a cell line that is not particularly sensitive to the FTI. The combination of FTI and epothilone represent a new potential clin. strategy for the treatment of advanced prostatic cancer.

IT **186692-73-9**, DesoxyEpothilone A **189453-10-9**, DesoxyEpothilone b
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microtubule-stabilizing agents epothilones A and B and derivs. induce mitotic arrest and apoptosis in human prostate cancer)
RN 186692-73-9 CAPLUS

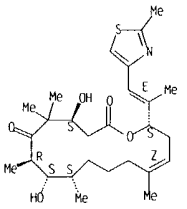
L5 ANSWER 90 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 91 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:126888 CAPLUS
DOCUMENT NUMBER: 130:196529
TITLE: Preparation of new epothilone derivatives as pharmaceutical agents
INVENTOR(S): Klar, Ulrich; Schwede, Wolfgang; Skuballa, Werner; Buchmann, Bernd; Schirner, Michael
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 185 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9907692	A2	19990218	WO 1998-EP5064	19980810 <--
WO 9907692	A3	19990514		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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DE 19751200	A1	19990520	DE 1997-19751200	19971113 <--
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AU 9893409	A1	19990301	AU 1998-93409	19980810 <--
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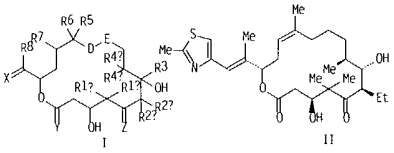
ZA 9810403	A	20000515	ZA 1998-10403	19981113 <--
US 2003144523	A1	20030731	US 2000-485292	20000503

PRIORITY APPLN. INFO.: DE 1997-19735574 A 19970809
DE 1997-19735575 A 19970809
DE 1997-19735578 A 19970809
DE 1997-19748928 A 19971024
DE 1997-19749717 A 19971031
DE 1997-19751200 A 19971113
DE 1998-19813821 A 19980320

L5 ANSWER 91 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
WO 1998-EP5064 W 19980810
OTHER SOURCE(S): MARPAT 130:196529
GRAPHIC IMAGE:



I II

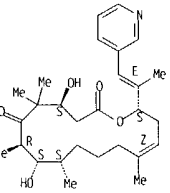
ABSTRACT:
Epothilone derivs. of formula I [X = O, alkylene-α,ω-dioxy, two alkoxy groups, etc.; Y = O, H2; Z = O, (H, OH), (H, protected OH); R1a, R1b = H, alkyl, aryl, aralkyl, or together = (CH2)m where m = 2, 3, 4, 5; R2a, R2b = H, alkyl, aryl, aralkyl, or together = (CH2)n where n = 2, 3, 4, 5; when D-E = CH2CH2 or when Y = O, R2a or R2b may not be H/Me; R3 = H, alkyl, aryl, aralkyl; R4a, R4b = H, alkyl, aryl, aralkyl, or together = (CH2)p where p = 2, 3, 4, 5; D-E = CH2CH2, CH:CH, C.tpibond.C, 2,3-oxiranediyl, CH(OH)CH(OH), CH(OH)CH2; R5 = H, alkyl, aryl, aralkyl; R6, R7 = H, together = a saturated bond or O; R8 = H, alkyl, aryl, aralkyl all of which may be substituted] are prepared. Thus, the title compds. (4S,7R,8S,9S,13E,16S(E))- and (4S,7R,8S,9S,13Z,16S(E))-4,8-dihydroxy-7-ethyl-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-1-oxa-5,5,9,13-tetramethylcyclohexadec-13-en-2,6-dione (II) were prepared in many steps. The new compds. interact with tubulin by stabilizing formed microtubuli. They are capable of influencing cell division in a phase-specific manner and are suitable for the treatment of malignant tumors, such as ovarian, gastric, colon, breast, lung, head and neck carcinoma, adenocarcinoma, malignant melanoma, and acute lymphocytic and myelocytic leukemia. They are also suited for anti-angiogenesis therapy and for the treatment of chronic inflammatory diseases (psoriasis, arthritis). To prevent uncontrolled cell growth on, and for better tolerability of, medical implants, the derivs. can be introduced into or applied to polymeric materials. The compds. provided for in the invention can be used alone or, to achieve additive or synergistic effects, in combination with other principles and substance categories used in tumor therapy.

IT **220773-51-3P 220773-57-9P 220773-58-0P**
220773-73-9P

L5 ANSWER 91 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of epothilone derivs. as antitumor agents)

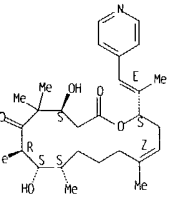
RN 220773-51-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 220773-57-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(4-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

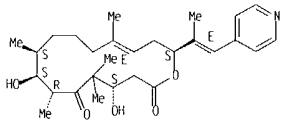
Absolute stereochemistry.
Double bond geometry as shown.



RN 220773-58-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-

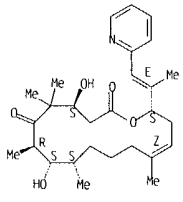
L5 ANSWER 91 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(4-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 220773-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

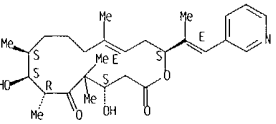


IT **220773-52-4P 220773-76-2P 220773-79-5P**
220776-27-2P 220776-28-3P 220776-42-1P
220776-43-2P 220776-48-7P 220776-49-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilone derivs. as antitumor agents)

RN 220773-52-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

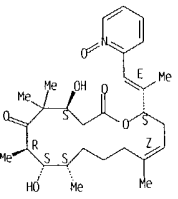
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 91 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 220773-76-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(1-oxido-2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

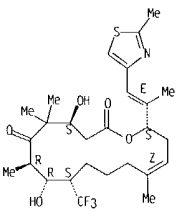
Absolute stereochemistry.
Double bond geometry as shown.



RN 220773-79-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

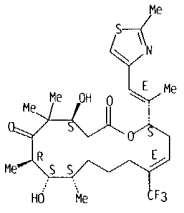
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 91 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 220776-42-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-(trifluoromethyl)-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

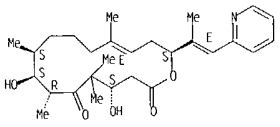
Absolute stereochemistry.
Double bond geometry as shown.



RN 220776-43-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-(trifluoromethyl)-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

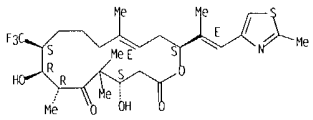
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 91 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 220776-27-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,13-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-9-(trifluoromethyl)-, (4S,7R,8R,9S,13E,16S)- (9CI) (CA INDEX NAME)

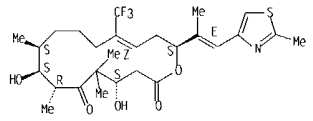
Absolute stereochemistry.
Double bond geometry as shown.



RN 220776-28-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,13-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-9-(trifluoromethyl)-, (4S,7R,8R,9S,13Z,16S)- (9CI) (CA INDEX NAME)

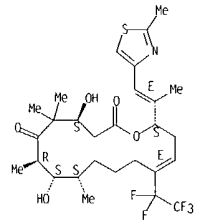
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 91 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



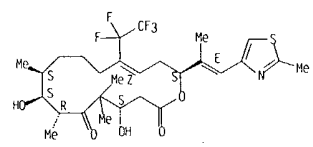
RN 220776-48-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-(pentafluoroethyl)-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 220776-49-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-(pentafluoroethyl)-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

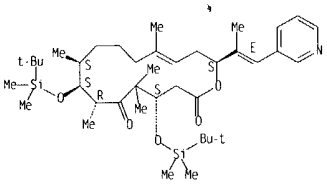
Absolute stereochemistry.
Double bond geometry as shown.



L5 ANSWER 91 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

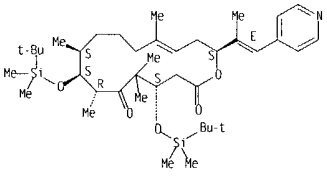
IT **220774-47-0P 220774-55-0P 220775-15-5P**
220775-17-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilone derivs. as antitumor agents)
RN 220774-47-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 220774-55-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(4-pyridinyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

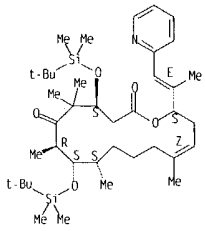
Absolute stereochemistry.
Double bond geometry as described by E or Z.



L5 ANSWER 91 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

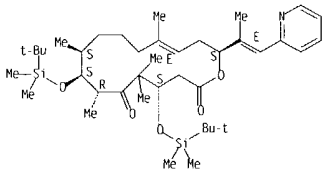
RN 220775-15-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 220775-17-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L5 ANSWER 92 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

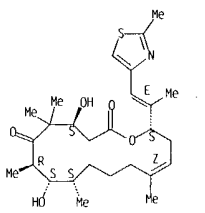
ACCESSION NUMBER:	1999:78939 CAPLUS
DOCUMENT NUMBER:	130:209528
TITLE:	A Highly Stereoselective Synthesis of Epothilone B
AUTHOR(S):	White, James D.; Carter, Rich G.; Sundermann, Kurt F.
CORPORATE SOURCE:	Department of Chemistry, Oregon State University, Corvallis, OR, OREGON, USA
SOURCE:	Journal of Organic Chemistry (**1999**), 64(3), 684-685 CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 130:209528
GRAPHIC IMAGE:	

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
A convergent synthesis of epothilone B (I) that generates all seven of its asym. centers in a completely stereoselective fashion is described. The key step is the coupling of phosphonium salt II with aldehyde III.

IT **189453-10-9P**, Desoxyepothilone B
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective convergent synthesis of epothilone B)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 92 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 93 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:64791 CAPLUS
DOCUMENT NUMBER: 130:139205
TITLE: syntheses of epothilone derivatives and intermediates for use in treatment of hyperproliferative cellular disease
INVENTOR(S): Vite, Gregory D.; Borzilleri, Robert M.; Kim, Soong-hoon; Johnson, James A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

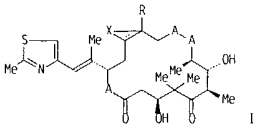
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902514	A2	19990121	WO 1998-US12550	19980616 <--
WO 9902514	A3	20010510		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6605599	B1	20030812	US 1998-84542	19980526
AU 9879720	A1	19990208	AU 1998-79720	19980616 <--
AU 731497	B2	20010329		
EP 1019389	A2	20000719	EP 1998-930300	19980616 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9810555	A	20000815	BR 1998-10555	19980616 <--
EE 200000013	A	20000815	EE 2000-200000013	19980616 <--
TR 200000065	T2	20001121	TR 2000-200000065	19980616 <--
NZ 501198	A	20010928	NZ 1998-501198	19980616 <--
JP 2002512634	T2	20020423	JP 1999-508673	19980616
RU 2213741	C2	20031010	RU 2000-102893	19980616
ZA 9805938	A	20000110	ZA 1998-5938	19980706 <--
MX 9911452	A	20000630	MX 1999-11452	19991209 <--
LT 4743	B	20001227	LT 1999-153	19991223 <--
NO 2000000076	A	20000107	NO 2000-76	20000107 <--
LV 12569	B	20010420	LV 2000-17	20000202 <--
US 2003220295	A1	20031127	US 2003-405886	20030403

PRIORITY APPLN. INFO.: US 1997-51951P P 19970708
US 1997-67524P P 19971204

L5 ANSWER 93 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 1998-84542 A1 19980526
WO 1998-US12550 W 19980616

OTHER SOURCE(S): MARPAT 130:139205
GRAPHIC IMAGE:



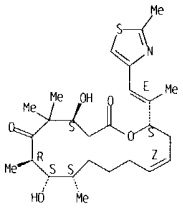
I

ABSTRACT:
Syntheses of epothilone derivs. (I) (R = H, Me; A = CH2, O, NH; X = H when bond double, α-epoxy when bond single) and intermediates for use in treatment of hyperproliferative cellular disease are described.

IT **186692-73-9P**, Epothilone C
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(syntheses of epothilone analogs and intermediates for use in treatment of hyperproliferative cellular disease)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

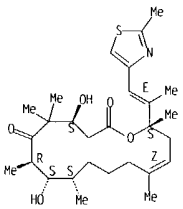
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 93 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



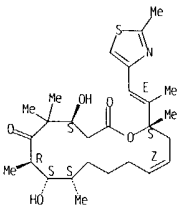
IT **219989-80-7 219989-81-8 219990-03-1 219990-04-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(syntheses of epothilone analogs and intermediates for use in treatment of hyperproliferative cellular disease)
RN 219989-80-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13,16-hexamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



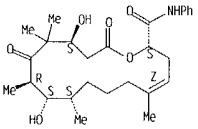
RN 219989-81-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,16-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

L5 ANSWER 93 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.
Double bond geometry as shown.



RN 219990-03-1 CAPLUS
CN Oxacyclohexadec-4-ene-2-carboxamide, 10,14-dihydroxy-5,9,11,13,13-pentamethyl-12,16-dioxo-N-phenyl-, (2S,4Z,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

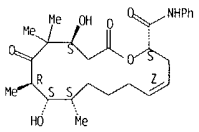
Absolute stereochemistry.
Double bond geometry as shown.



RN 219990-04-2 CAPLUS
CN Oxacyclohexadec-4-ene-2-carboxamide, 10,14-dihydroxy-9,11,13,13-tetramethyl-12,16-dioxo-N-phenyl-, (2S,4Z,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 93 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



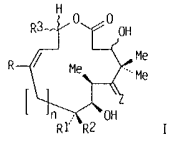
L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:48614 CAPLUS
DOCUMENT NUMBER: 130:124934
TITLE: Synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype
INVENTOR(S): Danishefsky, Samuel J.; Balog, Aaron; Bertinato, Peter; Su, Dai-Shi; Chou, Ting-Chau; Meng, Dong Fang; Kamenecka, Ted; Sorensen, Erik J.
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9901124	A1	19990114	WO 1997-US22381	19971203 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9857929	A1	19990125	AU 1998-57929	19971203 <--
AU 756699	B2	20030123		
EP 977563	A1	20000209	EP 1997-954055	19971203 <--
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
JP 2001507716	T2	20010612	JP 1999-501095	19971203 <--
EP 1386922	A2	20040204	EP 2003-22736	19971203
EP 1386922	A3	20040407		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
TW 504511	B	20021001	TW 1997-86118854	19980606
US 2003171596	A1	20030911	US 2002-58695	20020128
US 2004044221	A1	20040304	US 2003-374805	20030225
US 6723854	B2	20040420		
US 2004019089	A1	20040129	US 2003-431467	20030507
US 2004102495	A1	20040527	US 2003-695582	20031028

PRIORITY APPLN. INFO.:
US 1996-32282P P 19961203
US 1997-33767P P 19970114
US 1997-47566P P 19970522
US 1997-47941P P 19970529
US 1997-55533P P 19970813
EP 1997-954055 A3 19971203
US 1997-986025 A 19971203
WO 1997-US22381 W 19971203
US 2001-808451 A1 20010314
US 2001-874514 A1 20010605

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
US 2001-4571 A1 20011204
US 2002-58695 A1 20020128
US 2003-374805 A1 20030225
OTHER SOURCE(S): MARPAT 130:124934
GRAPHIC IMAGE:



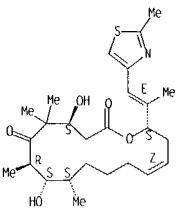
I

ABSTRACT:
Syntheses of epothilone A and B, desoxyepothilones A and B, and analogs (I) [R,R1,R2 = independently H, (un)substituted linear or branched chain alkyl; R3 = CHY=CHX, H, linear or branched chain alkyl, Ph, 2-methyl-1,3-thiazolinyl, 2-, 3-, or 4-furanyl, 2-, 3-, or 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3- or 6-indolyl; X = H, linear or branched chain alkyl, Ph, 2-methyl-1,3-thiazolinyl, 2-, 3-, or 4-furanyl, 2-, 3-, or 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3- or 6-indolyl; Y = H, linear or branched chain alkyl; Z = O, substituted NOH, substituted NNH2; n = 0-3] and their intermediates are described. Activities of novel compns. based on I and methods for the treatment of cancer and cancer which has developed a multidrug-resistant phenotype are presented.

IT **186692-73-9P 192370-82-4P 198475-04-6P**
198475-05-7P 219824-14-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

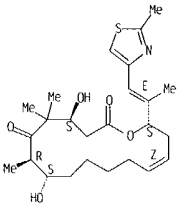
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 192370-82-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

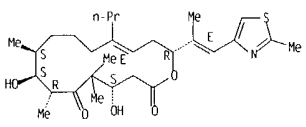
Absolute stereochemistry.
Double bond geometry as shown.



RN 198475-04-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

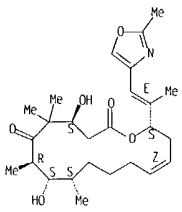
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **198475-12-6P 198475-13-7P 219823-99-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)
RN 198475-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

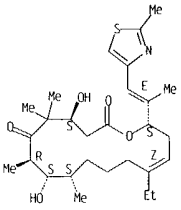
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198475-13-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

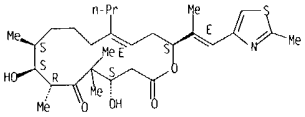
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-05-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

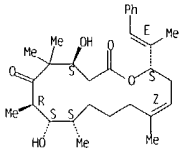
Absolute stereochemistry.
Double bond geometry as shown.



RN 219824-14-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16R)- (9CI) (CA INDEX NAME)

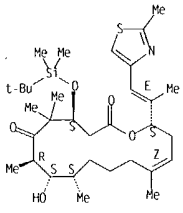
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 219823-99-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

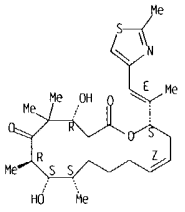
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **188259-95-2 188260-10-8 189453-10-9**
189453-40-5 198475-06-8 198475-07-9
198475-11-5 198475-18-2 219824-37-0
219824-38-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)
RN 188259-95-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

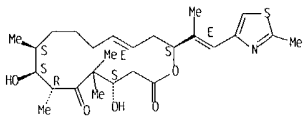
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

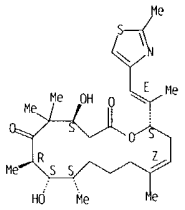
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

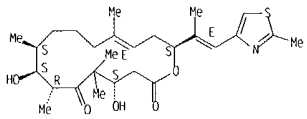
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

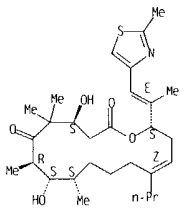
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198475-06-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

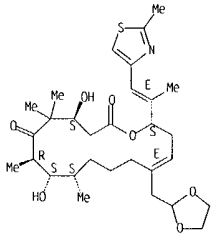
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-07-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(1,3-dioxolan-2-ylmethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

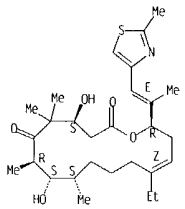
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198475-11-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16R)- (9CI) (CA INDEX NAME)

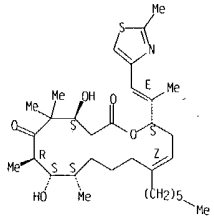
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-18-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-hexyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

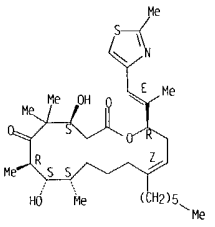
Absolute stereochemistry.
Double bond geometry as shown.



RN 219824-37-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-hexyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16R)- (9CI) (CA INDEX NAME)

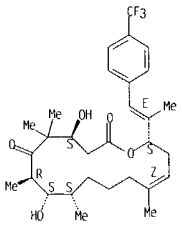
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 219824-38-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-[4-(trifluoromethyl)phenyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

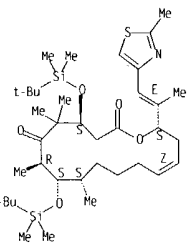
Absolute stereochemistry.
Double bond geometry as shown.



IT **186692-84-2P 189453-35-8P 192370-81-3P**
209261-05-2P 219824-09-6P 219824-13-2P
219824-19-8P 219824-25-6P 219824-29-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilones, intermediates and analogs for use in treatment of cancers with multidrug-resistant phenotype)
RN 186692-84-2 CAPLUS

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

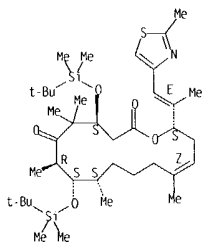
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

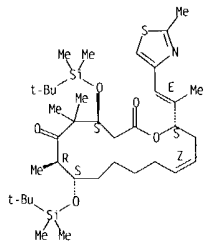
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 192370-81-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

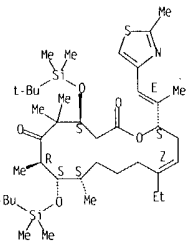
Absolute stereochemistry.
Double bond geometry as shown.



RN 209261-05-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-ethyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

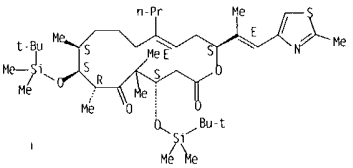
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 219824-09-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

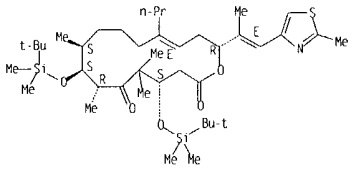
Absolute stereochemistry.
Double bond geometry as shown.



RN 219824-13-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16R)- (9CI) (CA INDEX NAME)

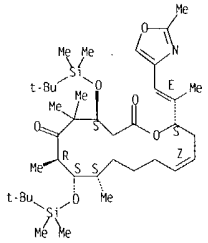
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 219824-19-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

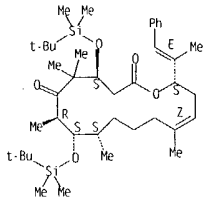
Absolute stereochemistry.
Double bond geometry as shown.



RN 219824-25-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

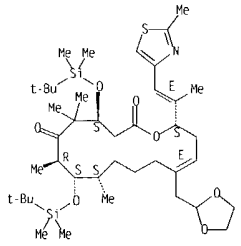
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 94 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 219824-29-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(1,3-dioxolan-2-ylmethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 95 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

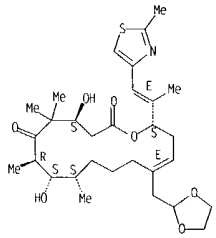
ACCESSION NUMBER: 1999:19340 CAPLUS
DOCUMENT NUMBER: 130:217758
TITLE: Desoxyepothilone B is curative against human tumor xenografts that are refractory to paclitaxel
AUTHOR(S): Chou, Ting-Chao; Zhang, Xiu-Guo; Harris, Christina R.; Kuduk, Scott D.; Balog, Aaron; Savin, Kenneth A.; Bertino, Joseph R.; Danishefsky, Samuel J.
CORPORATE SOURCE: Molecular Pharmacology and Therapeutics Program, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(26), 15798-15802
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The epothilones are naturally occurring, cytotoxic macrolides that function through a paclitaxel (Taxol)-like mechanism. Although structurally dissimilar, both classes of mols. lead to the arrest of cell division and eventual cell death by stabilizing cellular microtubule assemblies. The epothilones differ in their ability to retain activity against multidrug-resistant (MDR) cell lines and tumors where paclitaxel fails. In the current account, we focus on the relationship between epothilone and paclitaxel in the context of tumors with multiple drug resistance. The epothilone analog Z-12,13-desoxyepothilone B (dEpoB) is >35,000-fold more potent than paclitaxel in inhibiting cell growth in the MDR DC-3F/ADX cell line. Various formulations, routes, and schedules of i.v. administration of dEpoB have been tested in nude mice. Slow infusion with a Cremophor-ethanol vehicle proved to be the most beneficial in increasing efficacy and decreasing toxicity. Although dEpoB performed similarly to paclitaxel in sensitive tumors xenografts (MX-1 human mammary and HT-29 colon tumor), its effects were clearly superior against MDR tumors. When dEpoB was administered to nude mice bearing our MDR human lymphoblastic T cell leukemia (CCRF-CEM/paclitaxel), dEpoB demonstrated a full curative effect. For human mammary adenocarcinoma MCF-7/Adr cells refractory to paclitaxel, dEpoB reduced the established tumors, markedly suppressed tumor growth, and surpassed other commonly used chemotherapy drugs such as adriamycin, vinblastine, and etoposide in beneficial effects.

IT **198475-07-9 201136-64-3 221058-23-7 221058-24-8 221058-25-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(antitumor activity of desoxyepothilone B analogs)

RN 198475-07-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(1,3-dioxolan-2-ylmethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

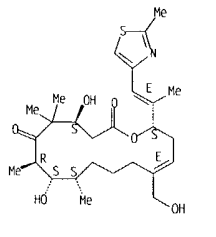
Absolute stereochemistry. Rotation (-).

L5 ANSWER 95 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



RN 201136-64-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

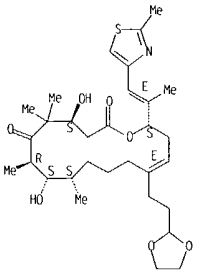
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 221058-23-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-[2-(1,3-dioxolan-2-yl)ethyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

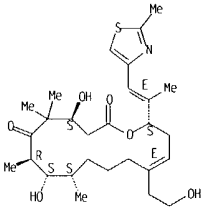
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 95 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 221058-24-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(2-hydroxyethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

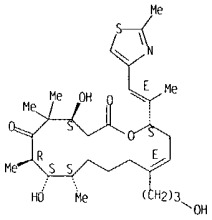
Absolute stereochemistry.
Double bond geometry as shown.



RN 221058-25-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(3-hydroxypropyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

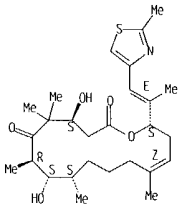
L5 ANSWER 95 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 95 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.
Double bond geometry as shown.



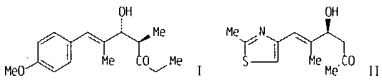
IT 189453-10-9, NSC 703147
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(desoxyepothilone B is curative against human tumor xenografts that are refractory to paclitaxel)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 96 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1998:805542 CAPLUS
DOCUMENT NUMBER:	130:153488
TITLE:	The antibody catalysis route to the total synthesis of epothilones
AUTHOR(S):	Sinha, Subhash C.; Barbas, Carlos F., III; Lerner, Richard A.
CORPORATE SOURCE:	The Skaggs Institute for Chemical Biology and the Department of Molecular Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE:	Proceedings of the National Academy of Sciences of the United States of America (1998), 95(25), 14603-14608 CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER:	National Academy of Sciences
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 130:153488
GRAPHIC IMAGE:	



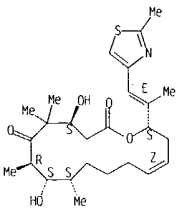
I II

ABSTRACT:
A total synthesis of epothilones A and C via antibody-catalyzed aldol and retro-aldol reactions was described. Epothilone precursors (+)-I and (-)-II were prepared using aldolase antibody 38C2 as a catalyst. These precursors were then converted to epothilones A and C to complete the total synthesis.

IT 186692-73-9P, Epothilone C
RL: BPN (Biosynthetic preparation); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of epothilones via antibody 38C2 catalyzed retro-aldol reactions)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 96 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 97 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:804132 CAPLUS
DOCUMENT NUMBER: 130:33009
TITLE: A method of treating cancer using an antineoplastic agent-prenyl-protein transferase inhibitor combination, and compound preparation
INVENTOR(S): Rosen, Neal; Sepp-lorenzino, Laura; Moasser, Mark M.; Oliff, Allen I.; Gibbs, Jackson B.; Kohl, Nancy; Graham, Samuel L.; Prendergast, George C.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Sloan-Kettering Institute for Cancer Research
SOURCE: PCT Int. Appl., 379 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

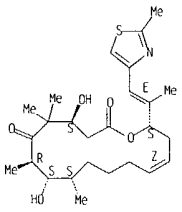
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854966	A1	19981210	WO 1998-US8646	19980604 <--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9877957	A1	19981221	AU 1998-77957	19980604 <--
EP 986302	A1	20000322	EP 1998-926029	19980604 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002503249	T2	20020129	JP 1999-502409	19980604
PRIORITY APPLN. INFO.:			US 1997-48736P	P 19970605
			GB 1998-1231	A 19980121
			WO 1998-US8646	W 19980604

ABSTRACT:
Methods are provided for treating cancer using a combination of a compound which is an antineoplastic agent and a compound which is a inhibitor of prenyl-protein transferase. The methods comprise administering to a mammal, either sequentially in any order or simultaneously, amts. of ≥2 therapeutic agents selected from a compound which is an antineoplastic agent and a compound which is an inhibitor or prenyl-protein transferase. The invention also relates to methods of preparing such compns.

IT **186692-73-9**, Desoxyepothilone A **189453-10-9**, Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

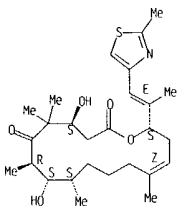
L5 ANSWER 97 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(Uses)
(antineoplastic agent-prenyl-protein transferase inhibitor combination for treating cancer, and compd. prepn.)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 97 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L5 ANSWER 98 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:762086 CAPLUS
DOCUMENT NUMBER: 129:343364
TITLE: Methods for preparation of epothilone derivatives
PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung m.b.H. (GBF), Germany
SOURCE: Ger. Offen., 2 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

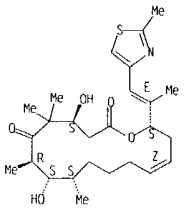
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19821954	A1	19981119	DE 1998-19821954	19980515 <--

PRIORITY APPLN. INFO.: DE 1997-19720250 19970515
OTHER SOURCE(S): MARPAT 129:343364
ABSTRACT:
Methods for preparation of epothilone derivs. are characterized by: (a) proceeding from epothilones A, B, C or D, wherein the C(2)- and C(3)-atoms can be joined together through CH2CH(OH) or CH:CH and wherein one provides an (un)protected OH group at the resulting bond at C(3) and C(7); (b) oxidation at C(16) to form a keto group; (c1) exchanging the oxygen of the keto-group to a :CH2 group using Ph3P:CH2; and if necessary (d1) this :CH2 group, with the help of the compound RCH:CH2, is catalytically converted to a :CHR group [R = aliphatic residue, (un)substituted Ph, heterocycle, especially a pharmaceutically active residue]; or (c2) for the bond between C(16) and C(17) in known ways provides the CH:CH2 group, and if necessary (d2) this group with the help of metathesis is converted into a :CHR group. Also claimed is the use of ozone to form the C(16) keto group. In addition, the reaction of the keto group with NaBH4 followed by tosyl chloride and base or a Bamford-Stevens reaction to form the methylene compound are claimed. Finally, rhodium, ruthenium, tungsten and molybdenum catalysts are claimed for the metathesis reactions.

IT **186692-73-9**, Epothilone C **189453-10-9**, Epothilone D
RL: RCT (Reactant); RACT (Reactant or reagent)
(methods for preparation of epothilone derivs.)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

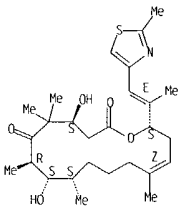
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 98 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

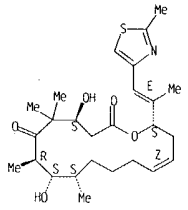
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 99 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:760826 CAPLUS
DOCUMENT NUMBER: 130:95407
TITLE: Derivatization of the C12-C13 functional groups of epothilones A, B and C
AUTHOR(S): Sefkow, Michael; Kiffe, Michael; Hofle, Gerhard
CORPORATE SOURCE: Gesellschaft fur Biotechnologische Forschung mbH, Abt. Naturstoffchemie, Braunschweig, D-38124, Germany
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(21), 3031-3036
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:95407
ABSTRACT:
Epothilone A reacted with hydrohalic acids to give C12-C13 halohydrin regioisomers (ratios: 2:1 - 4:1), whereas epothilone B gave under the same conditions the isomerically pure C12 halo C13 hydroxy derivative. With non-nucleophilic Bronstedt acids and with Lewis acids a highly solvent dependent product distribution and some unexpected rearrangement products were observed. Epothilone C bearing a double bond between C12 and C13 was regioselectively dihydroxylated or hydrogenated at that position.

IT **186692-73-9**, Epothilone C
RL: RCT (Reactant); RACT (Reactant or reagent)
(derivatization of the C12-C13 functional groups of epothilones A, B and C)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 99 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS

L5 ANSWER 100 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:760149 CAPLUS
DOCUMENT NUMBER: 130:29213
TITLE: Glycoconjugates of antitumor drugs with improved in vivo compatibility
INVENTOR(S): Bosslet, Klaus; Czech, Joerg; Gerken, Manfred; Straub, Rainer; Blumrich, Matthias
PATENT ASSIGNEE(S): Hoechst A.-G., Germany
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

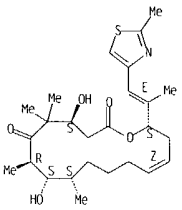
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19720312	A1	19981119	DE 1997-19720312	19970515 <--
EP 879605	A2	19981125	EP 1998-108041	19980502 <--
EP 879605	A3	19981202		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2237450	AA	19981115	CA 1998-2237450	19980513 <--
US 6020315	A	20000201	US 1998-76878	19980513 <--
CN 1199613	A	19981125	CN 1998-108475	19980514 <--
BR 9801632	A	19990629	BR 1998-1632	19980514 <--
AU 9866005	A1	19981119	AU 1998-66005	19980515 <--
AU 740694	B2	20011115		
JP 11029497	A2	19990202	JP 1998-133231	19980515 <--

PRIORITY APPLN. INFO.: DE 1997-19720312 A 19970515
OTHER SOURCE(S): MARPAT 130:29213
ABSTRACT:
A composition containing a conjugate Glycosyl-Y[C(:Y)X]pW(R)nXC(:Y)A (Glycosyl = enzymically cleavable poly-, oligo-, or monosaccharide; W = aromatic or heteroarom. residue, aliphatic residue with conjugated double bounds, or amino acid residue which cyclizes after cleavage of the glycosyl residue; R = H, Me, OMe, CO2H, CN, CO2Me, OH, NO2, F, Cl, Br,SO3H, SO2NH2, alkylsulfonamide; X = O, NH, CH2O, CH2NH, CH2NMe, etc.; Y = O, NH; A = antitumor agent; p = 0, 1; n = integer), a sugar and/or sugar alc., a divalent ion, and a pharmacol. acceptable carrier shows enhanced antitumor activity with decreased side effects compared to the unconjugated drug. Preferably the conjugate is more hydrophilic than the unconjugated drug, and the spacer group is spontaneously cleaved by chemical hydrolysis. Thus, i.v. administration of a composition containing N-[4-O-(β-D-glucopyranosyluronic acid)-3-nitrobenzyloxycarbonyl]doxorubici n Na salt (I) (400 mg/kg) in 0.9% NaCl solution containing 5% mannitol and CaCl2 to LoVo tumor-bearing mice on days 1, 4, and 8 considerably slowed tumor growth and decreased mortality compared to controls receiving I alone or combined only with mannitol.

L5 ANSWER 100 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **186692-73-9D**, Epothilone C, glycoconjugates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycoconjugates of antitumor drugs with improved in vivo compatibility)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

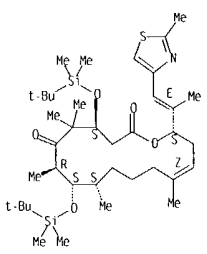
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L5 ANSWER 101 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:732784 CAPLUS
DOCUMENT NUMBER: 130:81320
TITLE: Easy access to the epothilone family - synthesis of epothilone B
AUTHOR(S): Mulzer, Johann; Mantoulidis, Andreas; Öhler, Elisabeth
CORPORATE SOURCE: Inst. fur Organische Chemie, Univ. Wien, Vienna, A-1090, Austria
SOURCE: Tetrahedron Letters (1998), 39(47), 8633-8636
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:81320
ABSTRACT:
An easy access to four out of five naturally occurring epothilones (A-E) is reported. Key steps are an enantioselective Mukaiyama type aldol reaction, (E)- and (Z)-selective olefinations, and a sulfone alkylation.

IT **189453-35-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilone B)
RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

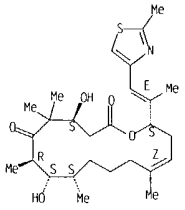
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **189453-10-9P**, Epothilone D
RL: SPN (Synthetic preparation); PREP (Preparation)

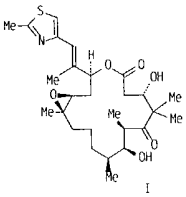
L5 ANSWER 101 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(synthesis of epothilone B)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

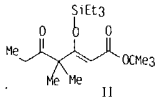


REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 102 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:726876 CAPLUS
DOCUMENT NUMBER: 130:81319
TITLE: A novel aldol condensation with 2-methyl-4-pentenal and its application to an improved total synthesis of epothilone B
AUTHOR(S): Balog, Aaron; Harris, Christina; Savin, Kenneth; Zhang, Xiu-Guo; Chou, Ting Chao; Danishefsky, Samuel J.
CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Angewandte Chemie, International Edition (1998), 37(19), 2675-2678
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:81319
GRAPHIC IMAGE:



I

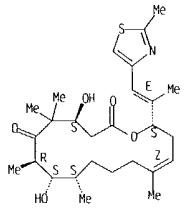


II

ABSTRACT:
Epothilone B was prepared in 9 steps via aldol condensation of (S)-2-methyl-4-pentenal with the enolate I.

IT **218924-18-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(novel aldol condensation with 2-methyl-4-pentenal and application to improved total synthesis of epothilone B)

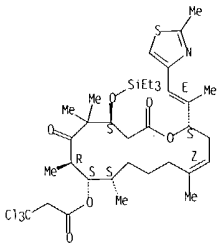
L5 ANSWER 102 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 102 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 218924-18-6 CAPLUS
CN Propanoic acid, 3,3,3-trichloro-, (4S,7R,8S,9S,13Z,16S)-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-2,6-dioxo-4-[(triethylsilyl)oxy]oxacyclohexadec-13-en-8-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **189453-10-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(novel aldol condensation with 2-methyl-4-pentenal and application to improved total synthesis of epothilone B)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

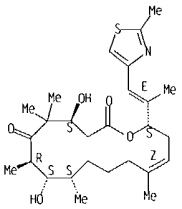
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 103 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:534644 CAPLUS
DOCUMENT NUMBER: 129:239597
TITLE: Desoxyepothilone B: an efficacious microtubule-targeted antitumor agent with a promising in vivo profile relative to epothilone B
AUTHOR(S): Chou, Ting-Chao; Zhang, Xiu-Guo; Balog, Aaron; Su, Dai-Shi; Meng, Dongfang; Savin, Kenneth; Bertino, Joseph R.; Danishefsky, Samuel J.
CORPORATE SOURCE: Molecular Pharmacology and Therapeutics Program, Cornell University Graduate School of Medical Sciences, New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(16), 9642-9647
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
A new class of 16-membered macrolides, the epothilones (Epos), has been synthesized and evaluated for antitumor potential in vitro and in vivo. Recent studies in these and other labs. showed that epothilones and paclitaxel (paclitaxel) share similar mechanisms of action in stabilizing microtubule arrays as indicated by binding-displacement studies, substitution for paclitaxel in paclitaxel-dependent cell growth, and electron microscopic examns. The present study examined cell growth-inhibitory effects in two rodent and three human tumor cell lines and their drug-resistant sublines. Although paclitaxel showed as much as 1,970-fold cross-resistance to the sublines resistant to paclitaxel, adriamycin, vinblastine, or actinomycin D, most epothilones exhibit little or no cross-resistance. In multidrug-resistant CCRF-CEM/VBL100 cells, IC50 values for EpoA (1), EpoB (2), desoxyEpoA (3) (dEpoA), desoxyEpoB (4) (dEpoB), and paclitaxel were 0.02, 0.002, 0.012, 0.017, and 4.14 μM, resp. In vivo studies, using i.p. administration, indicated that the parent, EpoB, was highly toxic to mice and showed little therapeutic effect when compared with a lead compound, dEpoB. More significantly, dEpoB (25-40 mg/kg, Q2Dx5, i.p.) showed far superior therapeutic effects and lower toxicity than paclitaxel, doxorubicin, camptothecin, or vinblastine (at maximal tolerated doses) in parallel expts. For mammary adenocarcinoma xenografts resistant to adriamycin, MCF-7/Adr, superior therapeutic effects were obtained with dEpoB compared with paclitaxel when i.p. regimens were used. For ovarian adenocarcinoma xenografts, SK-OV-3, dEpoB (i.p.), and paclitaxel (i.v.) gave similar therapeutic effects. In nude mice bearing a human mammary carcinoma xenograft (MX-1), marked tumor regression and cures were obtained with dEpoB.

IT **189453-10-9**, Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(desoxyepothilone B is an efficacious microtubule-targeted antitumor agent with a promising in vivo profile relative to epothilone B)
RN 189453-10-9 CAPLUS

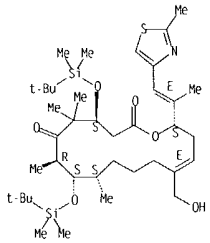
L5 ANSWER 103 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 104 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



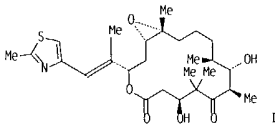
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 104 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:503765 CAPLUS
DOCUMENT NUMBER: 129:244965
TITLE: Synthesis and biological properties of C12,13-cyclopropyl-epothilone A and related epothilones
AUTHOR(S): Nicolaou, K. C.; Finlay, M. Ray V.; Ninkovic, Sacha; King, N. Paul; He, Yun; Li, Tianhu; Sarabia, Francisco; Vourloumis, Dionisios
CORPORATE SOURCE: Dep. Chemistry, The Skaggs Inst. Chem. Biol., The Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: Chemistry & Biology (1998), 5(7), 365-372
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Current Biology Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:244965
ABSTRACT:
Background: The epothilones are natural substances that are potently cytotoxic, having an almost identical mode of action to Taxol as tubulin-polymerization and microtubule-stabilizing agents. The development of detailed structure-activity relationships for these compds. and the further elucidation of their mechanism of action is of high priority. Results: The chemical synthesis of the C12,13-cyclopropyl analog of epothilone A and its C12,13-trans-diastereoisomer has been accomplished. These compds. and several other epothilone analogs have been screened for their ability to induce tubulin polymerization and death of a number of tumor cells. Several interesting structure-activity trends within this family of compds. were identified. Conclusions: The results of the biol. tests conducted in this study have demonstrated that, although a number of positions on the epothilone skeleton are amenable to modification without significant loss of biol. activity, the replacement of the epoxide moiety of epothilone A with a cyclopropyl group leads to total loss of activity.

IT **209260-82-2**
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(synthesis and biol. properties of C12,13-cyclopropyl-epothilone A and related epothilones)
RN 209260-82-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 105 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:492150 CAPLUS
DOCUMENT NUMBER: 129:216449
TITLE: Total synthesis of (-)-epothilone B
AUTHOR(S): May, Scott A.; Grieco, Paul A.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Montana State University, Bozeman, MT, 59717, USA
SOURCE: Chemical Communications (Cambridge) (1998), (15), 1597-1598
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:



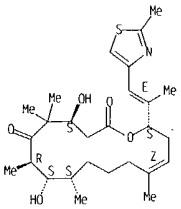
I

ABSTRACT:
The sixteen-membered ring macrolide (-)-epothilone B (I) has been synthesized by a route which features stereospecific methylation of an (E)-γ,δ-epoxy acrylate, the use of a double asym. reaction employing (R,R)-diisopropyltartrate and (E)-crotylboronate, ring closure by means of an olefin metathesis reaction.

IT **189453-10-9P 204195-20-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (-)-epothilone B)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

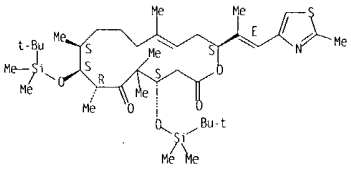
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 105 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204195-20-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

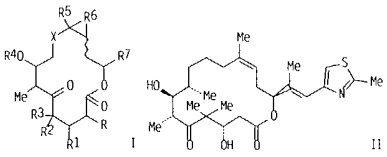
ACCESSION NUMBER: 1998:405952 CAPLUS
DOCUMENT NUMBER: 129:81625
TITLE: Preparation of epothilone analogs as anticancer agents
INVENTOR(S): Nicolaou, Costa Kyriacos; He, Yun; Ninkovic, Sacha; Pastor, Joaquin; Roschangar, Frank; Sarabia, Francisco; Vallberg, Hans; Vourloumis, Dionisios; Winssinger, Nicolas; Yang, Zhen; King, Nigel Paul; et al.
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Scripps Research Institute
SOURCE: PCT Int. Appl., 213 pp.
CODEN: PIXXO2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9825929	A1	19980618	WO 1997-EP7011	19971212 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6441186	B1	20020827	US 1997-923869	19970904
AU 9857577	A1	19980703	AU 1998-57577	19971212 <--
AU 746597	B2	20020502		
EP 944634	A1	19990929	EP 1997-953808	19971212 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9714140	A	20000229	BR 1997-14140	19971212 <--
JP 2001504856	T2	20010410	JP 1998-526247	19971212 <--
US 6660758	B1	20031209	US 1999-319885	19990924

PRIORITY APPLN. INFO.: US 1996-32864P P 19961213
US 1997-856533 A 19970514
US 1997-923869 A2 19970904
WO 1997-EP7011 W 19971212

OTHER SOURCE(S): MARPAT 129:81625
GRAPHIC IMAGE:

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



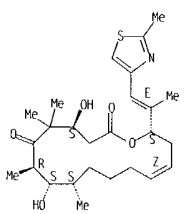
ABSTRACT:
Epothilone A, epothilone B, analogs of epothilone and libraries of epothilone analogs of formula I [X = (CH2)n; n = 1-5; R1 = OH, OMe, absent; R2, R3 = H, CH2, Me; R4 = H, Me, protecting group; R5 = H, Me, CHO, (substituted) CO2H, etc.; R6 = O, CH2, absent; R7 = thiazolealkyl, etc.] are synthesized. Epothilone A and B are known anticancer agents that derive their anticancer activity by the prevention of mitosis through the induction and stabilization of microtubulin assembly. Several of the analogs are demonstrated to have a superior cytotoxic activity as compared to epothilone A or epothilone B as demonstrated by their enhanced ability to induce the polymerization and stabilization of microtubules. Thus, II was prepared and was shown to induce tubulin polymerization at 94% relative to GTP, and inhibit carcinoma cell growth.

IT **186692-73-9P 187283-52-9P 188260-10-8P**
189453-10-9P 189453-40-5P 193071-86-2P
193146-35-9P 198475-12-6P 198571-09-4P
198571-10-7P 198571-11-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of epothilone analogs as anticancer agents)

RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

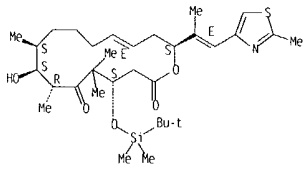
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 187283-52-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

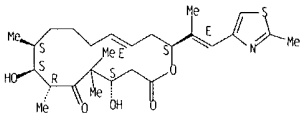
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

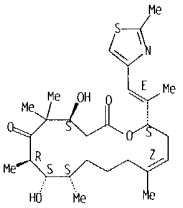
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

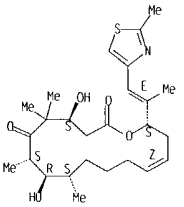
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

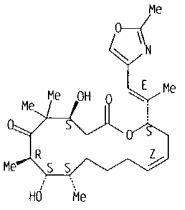
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

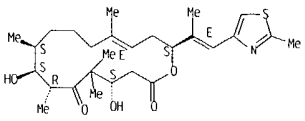
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-09-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

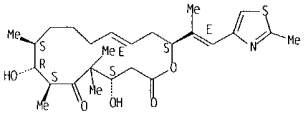
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 193071-86-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

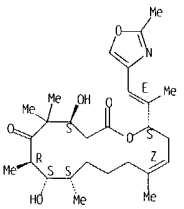
Absolute stereochemistry.
Double bond geometry as shown.



RN 193146-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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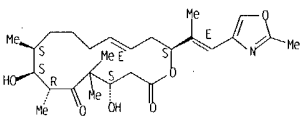
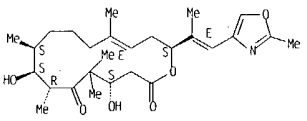
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-11-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **188259-95-2P 188260-34-6P 192370-82-4P**

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

198571-04-9P 198571-15-2P 198571-16-3P
198571-17-4P 198571-18-5P 198571-19-6P
198571-20-9P 198571-21-0P 198571-22-1P
198571-24-3P 198571-25-4P 198571-26-5P
198571-28-7P 198571-29-8P 198571-30-1P
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198571-76-5P 198571-77-6P 198571-78-7P
201136-87-0P 201136-94-9P 204513-12-2P
204513-14-4P 204513-35-9P 204513-36-0P
204513-37-1P 204513-38-2P 204513-39-3P
204513-40-6P 204513-41-7P 204513-42-8P
204513-43-9P 204513-44-0P 204513-45-1P
204513-46-2P 204513-47-3P 204513-48-4P
204513-49-5P 204513-50-8P 204513-51-9P
204513-52-0P 204513-53-1P 204513-54-2P
209260-87-7P 209260-88-8P 209260-89-9P
209260-90-2P 209260-91-3P 209260-92-4P
209260-93-5P 209260-94-6P 209260-95-7P
209260-96-8P 209260-97-9P 209260-98-0P

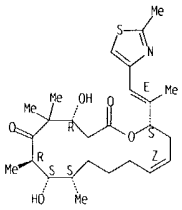
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of epothilone analogs as anticancer agents)

RN 188259-95-2 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

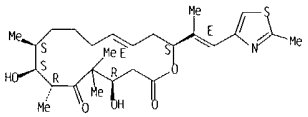
L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 188260-34-6 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

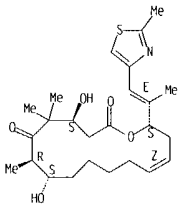


RN 192370-82-4 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

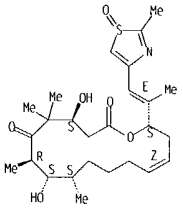
L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-04-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-1-oxido-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

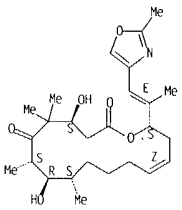


RN 198571-15-2 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

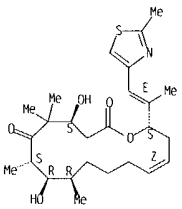
L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-16-3 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9R,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

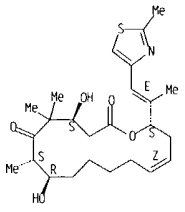


RN 198571-17-4 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,13Z,16S)- (9CI) (CA INDEX NAME)

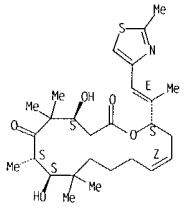
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-18-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

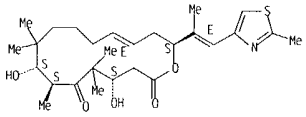


RN 198571-19-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

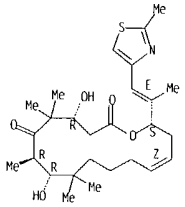
L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-24-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8R,13Z,16S)-(9CI) (CA INDEX NAME)

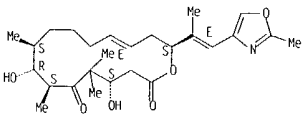
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-25-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9R,13E,16S)-(9CI) (CA INDEX NAME)

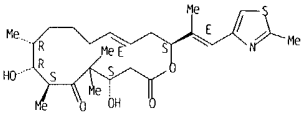
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



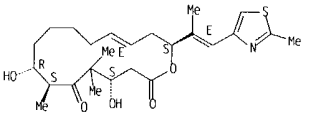
RN 198571-20-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



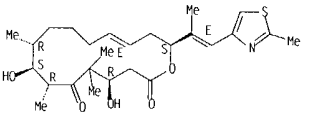
RN 198571-21-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



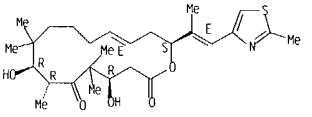
RN 198571-22-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8S,13E,16S)-

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



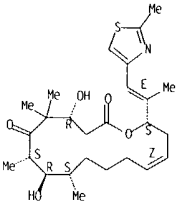
RN 198571-26-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-28-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

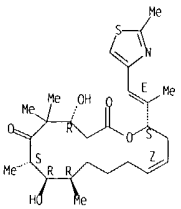
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-29-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-

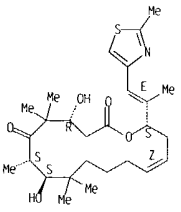
L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4R.7S.8R.9R.13Z.16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-30-1 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9.9-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4R.7S.8S.13Z.16S)-
(9CI) (CA INDEX NAME)

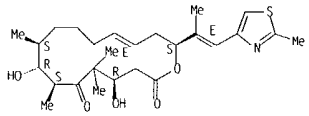
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-31-2 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4R.7S.8R.9S.13E.16S)-

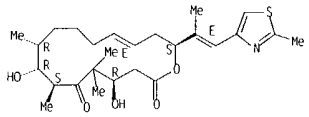
L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



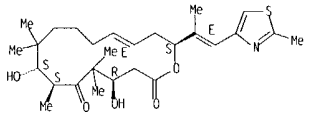
RN 198571-32-3 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4R.7S.8R.9R.13E.16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-33-4 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9.9-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4R.7S.8S.13E.16S)-
(9CI) (CA INDEX NAME)

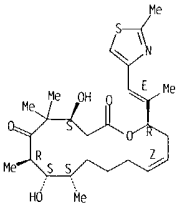
Absolute stereochemistry.
Double bond geometry as shown.



L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

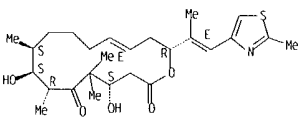
RN 198571-37-8 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13Z.16R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-38-9 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13E.16R)-
(9CI) (CA INDEX NAME)

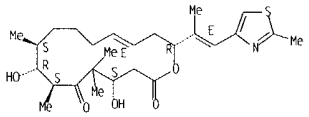
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-39-0 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7S.8R.9S.13E.16R)-
(9CI) (CA INDEX NAME)

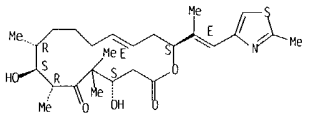
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



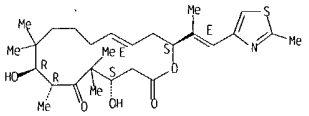
RN 198571-66-3 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9R.13E.16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-67-4 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9.9-pentamethyl-16-
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8R.13E.16S)-
(9CI) (CA INDEX NAME)

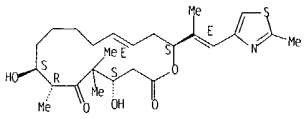
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-68-5 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7-trimethyl-16-[(1E)-1-
methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.13E.16S)- (9CI) (CA
INDEX NAME)

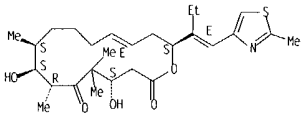
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-69-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-[(2-methyl-4-thiazolyl)methylene]propyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

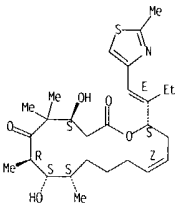
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-70-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13Z,16S)-(9CI) (CA INDEX NAME)

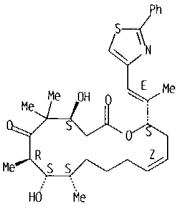
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-73-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

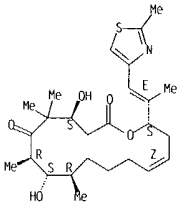
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-74-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

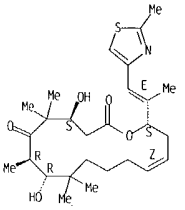
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-71-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8R,13Z,16S)-(9CI) (CA INDEX NAME)

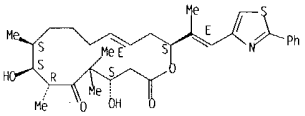
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-72-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-[(2-methyl-4-thiazolyl)methylene]propyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

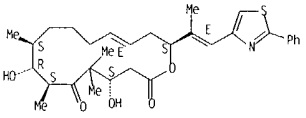
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



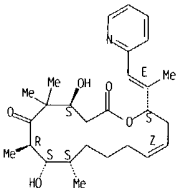
RN 198571-76-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-77-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

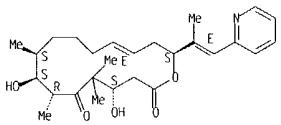
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-78-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-

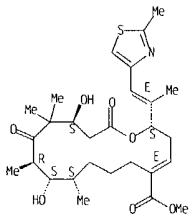
L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 201136-87-0 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxylic acid, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, methyl ester, (2S.4E.9S.10S.11R.14S)- (9CI) (CA INDEX NAME)

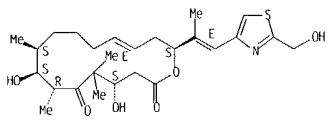
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-94-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethynyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

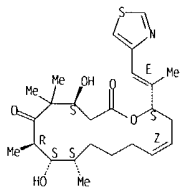
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



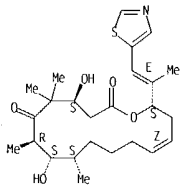
RN 204513-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-, (4S.7R.8S.9S.13Z.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

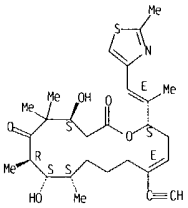


RN 204513-36-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-, (4S.7R.8S.9S.13Z.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

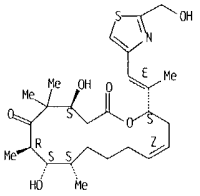


L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-12-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S.7R.8S.9S.13Z.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



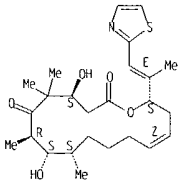
RN 204513-14-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

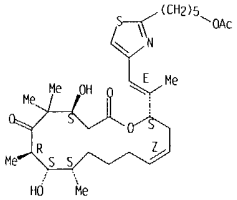
RN 204513-37-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thiazolyl)ethenyl]-, (4S.7R.8S.9S.13Z.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-38-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[5-(acetyloxy)pentyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S.7R.8S.9S.13Z.16S)- (9CI) (CA INDEX NAME)

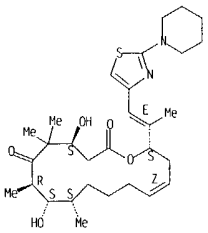
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-39-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(1-piperidinyl)-4-thiazolyl]ethenyl]-, (4S.7R.8S.9S.13Z.16S)- (9CI) (CA INDEX NAME)

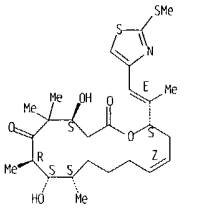
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-40-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

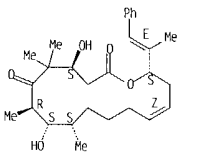
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-41-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

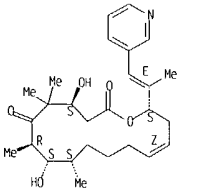
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



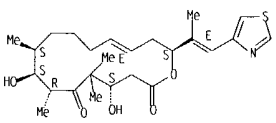
RN 204513-44-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

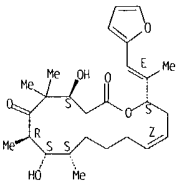


RN 204513-45-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

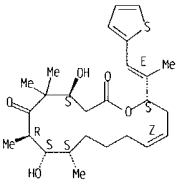


L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-42-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

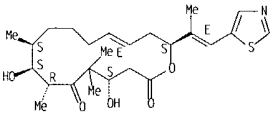


RN 204513-43-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

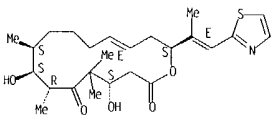
L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 204513-46-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



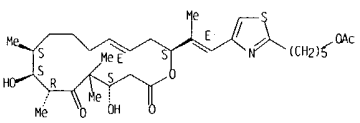
RN 204513-47-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



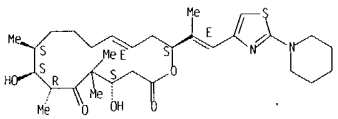
RN 204513-48-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[5-(acetyloxy)pentyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



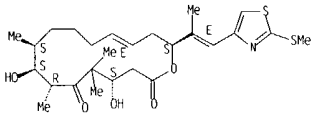
L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 204513-49-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(1-piperidinyl)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-50-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

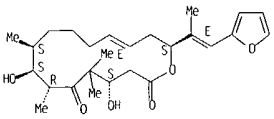
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-51-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

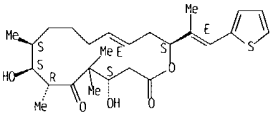
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



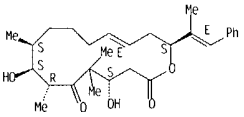
RN 204513-52-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-53-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

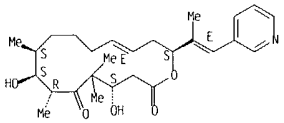
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-54-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA

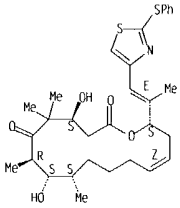
L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-87-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(phenylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

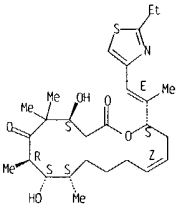
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-88-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethyl-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

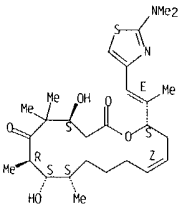
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 209260-89-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(dimethylamino)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

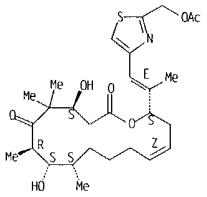
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-90-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[(acetyloxy)methyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

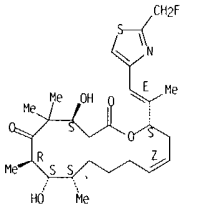
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 209260-91-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

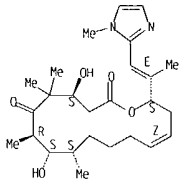
Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-92-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(1-methyl-1H-imidazol-2-yl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

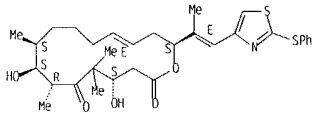
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



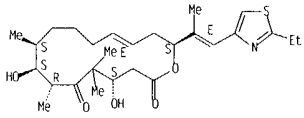
RN 209260-93-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(phenylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-94-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-ethyl-4-thiazolyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

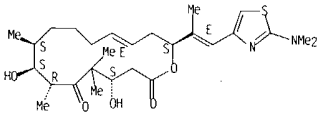
Absolute stereochemistry.
Double bond geometry as shown.



L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

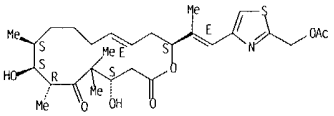
RN 209260-95-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(dimethylamino)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



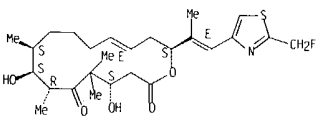
RN 209260-96-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[(acetyloxy)methyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 209260-97-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-(fluoromethyl)-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

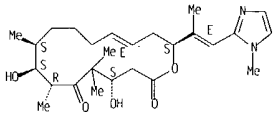
Absolute stereochemistry.
Double bond geometry as shown.



L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 209260-98-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(1-methyl-1H-imidazol-2-yl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

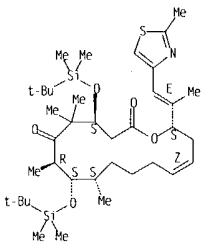


IT **186692-84-2P 187283-49-4P 189453-35-8P**
190370-08-2P 193146-34-8P 198475-04-6P
201136-64-3P 201136-85-8P 201136-86-9P
201136-88-1P 202333-40-2P 202333-45-7P
203252-73-7P 203252-74-8P 204513-16-6P
204513-26-8P 204513-28-0P 204513-30-4P
209260-71-9P 209260-82-2P 209260-83-3P
209260-85-5P 209260-99-1P 209261-03-0P
209261-04-1P 209261-05-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilone analogs as anticancer agents)

RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

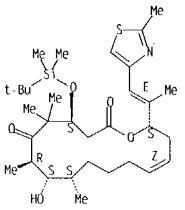
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



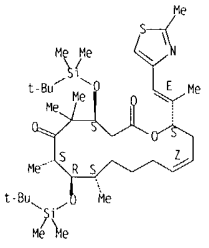
RN 187283-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



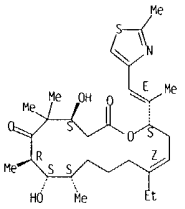
RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198475-04-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

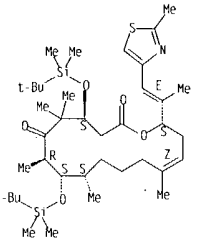
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-64-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

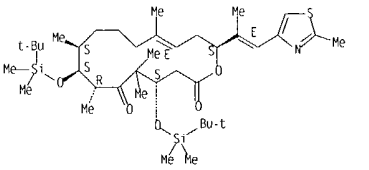
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



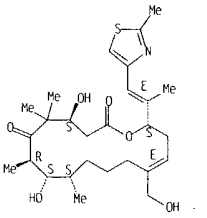
RN 190370-08-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



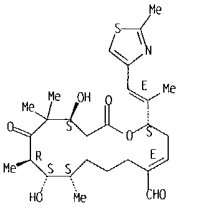
RN 193146-34-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-85-8 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxaldehyde, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

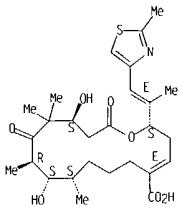
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-86-9 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxylic acid, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

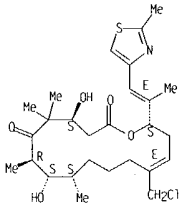
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-88-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(chloromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

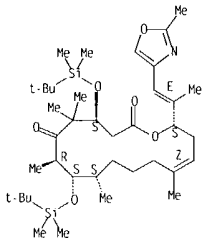
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 202333-40-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

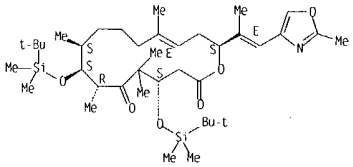
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 203252-74-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

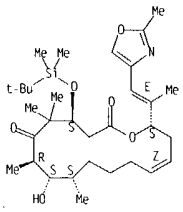
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 204513-16-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

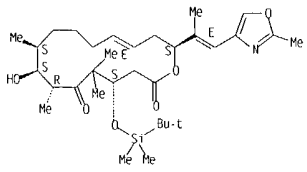
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 202333-45-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

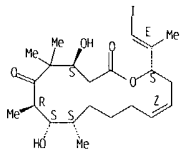
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 203252-73-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

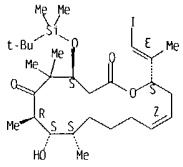
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



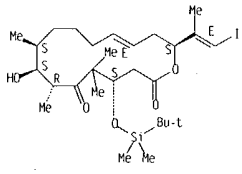
RN 204513-26-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-28-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

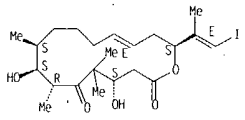
Absolute stereochemistry.
Double bond geometry as shown.



L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

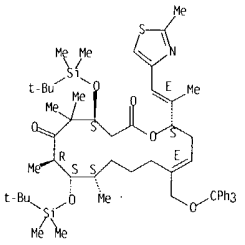
RN 204513-30-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



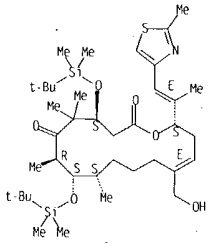
RN 209260-71-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-[(triphenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 209260-82-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

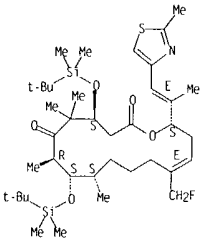
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 209260-83-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(fluoromethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

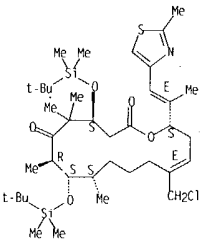
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 209260-85-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(chloromethyl)-4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

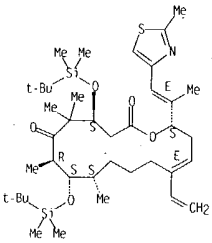
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 209260-99-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-ethenyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

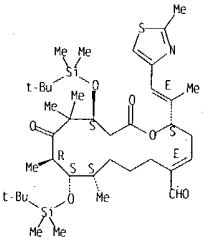
Absolute stereochemistry. Rotation (-).

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



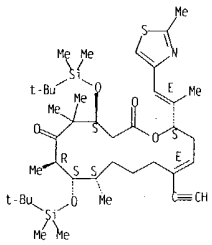
RN 209261-03-0 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxaldehyde, 10,14-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



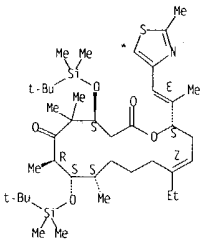
RN 209261-04-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-ethynyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 106 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



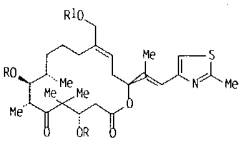
RN 209261-05-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-ethyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:378435 CAPLUS
DOCUMENT NUMBER: 129:189151
TITLE: Total synthesis of 26-hydroxy-epothilone B and related analogs via a macrolactonization based strategy
AUTHOR(S): Nicolaou, K. C.; Finlay, M. Ray V.; Ninkovic, Sacha; Sarabia, Francisco
CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Tetrahedron (1998), 54(25), 7127-7166
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:189151
GRAPHIC IMAGE:



I

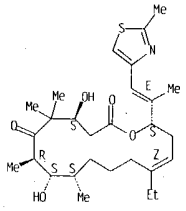
ABSTRACT:
The chemical synthesis of a series of 26-substituted epothilones B was described. Fully protected 26-hydroxydesoxy-epothilone B I (R = SiMe2CMe3, R1 = CPh3), prepared via a macrolactonization strategy, served as a common precursor to the designed epothilones described. The synthesized compds. were members of a large epothilone library of a number of antitumor agents.

IT **198475-04-6P 201136-64-3P**, (-)-26-Hydroxydesoxyepothilone B **201136-85-8P 201136-86-9P 209260-71-9P 209260-82-2P 209260-83-3P 209260-85-5P 209260-99-1P 209261-03-0P 209261-04-1P 209261-05-2P 211801-57-9P 211801-61-5P 211801-80-8P 211801-81-9P 211801-82-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of 26-hydroxy-epothilone B and related analogs via a macrolactonization based strategy)

RN 198475-04-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-

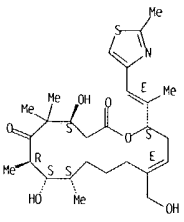
tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-64-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

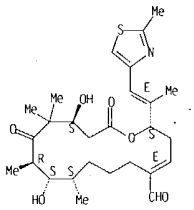
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-85-8 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxaldehyde, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)-, (9CI) (CA INDEX NAME)

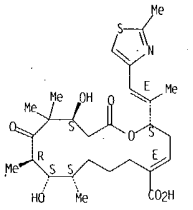
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-86-9 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxylic acid, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

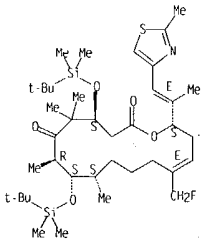


RN 209260-71-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-[(triphenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

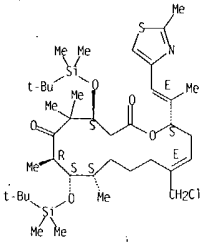
L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



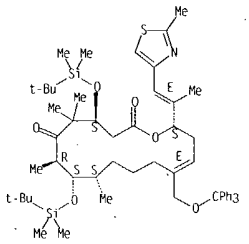
RN 209260-85-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(chloromethyl)-4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



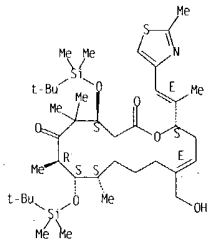
RN 209260-99-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-

L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 209260-82-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

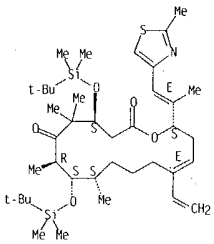
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 209260-83-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(fluoromethyl)-5,5,7,9-tetramethyl-16-

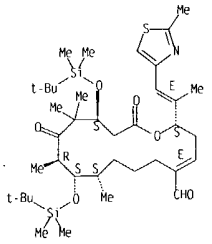
L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
dimethylethyl)dimethylsilyl]oxy]-13-ethenyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 209261-03-0 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxaldehyde, 10,14-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

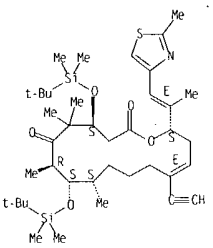
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 209261-04-1 CAPLUS

L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-ethynyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

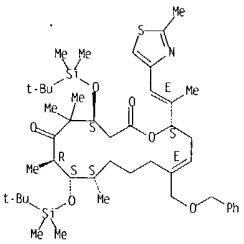


RN 209261-05-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-ethyl-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(2-methyl-4-thiazolyl)ethenyl]-13-[(phenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

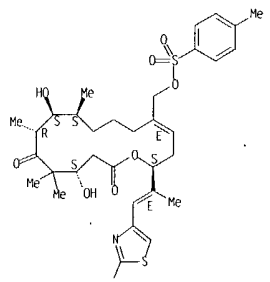
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



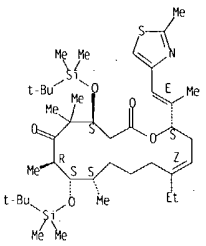
RN 211801-80-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-[[[(4-methylphenyl)sulfonyl]oxy]methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

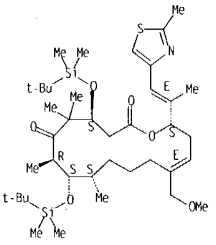


L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 211801-57-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-(methoxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



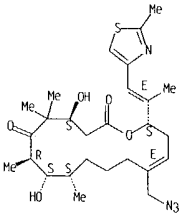
RN 211801-61-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-

L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

RN 211801-81-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(azidomethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

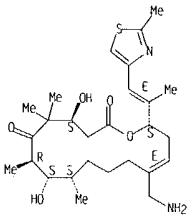
Absolute stereochemistry.
Double bond geometry as shown.



RN 211801-82-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(aminomethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

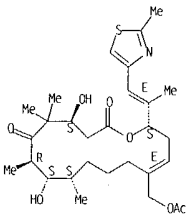
L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **201136-81-4P 201136-83-6P 201136-84-7P**
201136-87-0P 201136-88-1P 201136-89-2P
201136-90-5P 201136-91-6P 201136-92-7P
201136-93-8P 201136-94-9P 211801-71-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of 26-hydroxy-epothilone B and related analogs via a macrolactonization based strategy)

RN 201136-81-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-[(acetyloxy)methyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

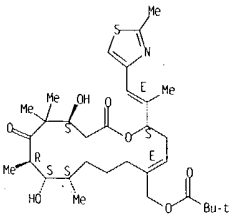
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-83-6 CAPLUS

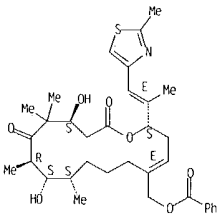
L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Propanoic acid, 2,2-dimethyl-, [(2S,4E,9S,10S,11R,14S)-10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxooxacyclohexadec-4-en-5-yl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-84-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-[(benzoyloxy)methyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

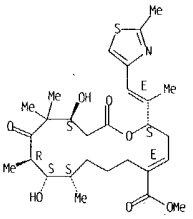
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-87-0 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxylic acid, 10,14-dihydroxy-9,11,13,13-

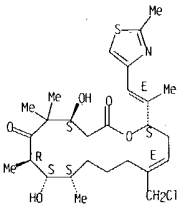
L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, methyl ester, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-88-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(chloromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

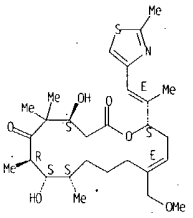
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-89-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(methoxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

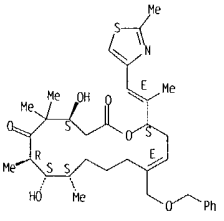
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-90-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-[(phenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

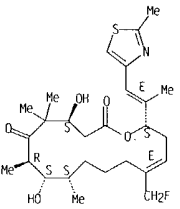
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-91-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(fluoromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

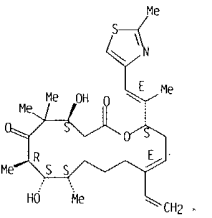
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-92-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethenyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

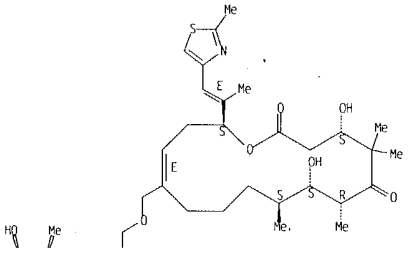


RN 201136-93-8 CAPLUS
CN Acetamide, N-[[(2S,4E,9S,10S,11R,14S)-10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxooxacyclohexadec-4-en-5-yl]methyl]- (9CI) (CA INDEX NAME)

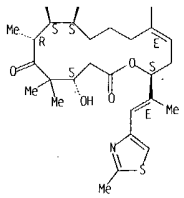
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

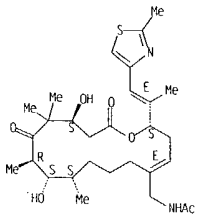


PAGE 2-A



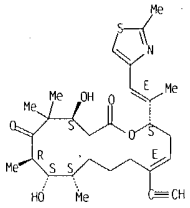
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 107 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-94-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethynyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 211801-71-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13,13'-[oxybis(methylene)]bis[4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,4'S,7R,7'R,8S,8'S,9S,9'S,13E,13'E,16S,16'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 108 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

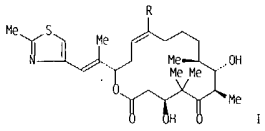
ACCESSION NUMBER: 1998:352834 CAPLUS
DOCUMENT NUMBER: 129:53436
TITLE: Epothilone C, D, E and F, production process, and their use as cytostatics well as phytosanitary agents
INVENTOR(S): Reichenbach, Hans; Hofle, Gerhard; Gerth, Klaus; Steinmetz, Heinrich
PATENT ASSIGNEE(S): Gesellschaft Fur Biotechnologische Forschung m.b.H. (GBF), Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9822461	A1	19980528	WO 1997-EP6442	19971118 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9854837	A1	19980610	AU 1998-54837	19971118 <--
AU 753546	B2	20021024		
ZA 9710384	A	19990518	ZA 1997-10384	19971118 <--
EP 941227	A1	19990915	EP 1997-951233	19971118 <--
EP 941227	B1	20040519		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1237970	A	19991208	CN 1997-199814	19971118 <--
BR 9713363	A	20000125	BR 1997-13363	19971118 <--
NZ 335383	A	20001027	NZ 1997-335383	19971118 <--
JP 2001504474	T2	20010403	JP 1998-523208	19971118 <--
IL 129558	A1	20011031	IL 1997-129558	19971118 <--
RU 2198173	C2	20030210	RU 1999-113031	19971118
EP 1367057	A1	20031203	EP 2003-16552	19971118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
TW 408119	B	20001011	TW 1997-86117334	19980121 <--
NO 9902338	A	19990514	NO 1999-2338	19990514 <--
KR 2000053308	A	20000825	KR 1999-704302	19990514 <--

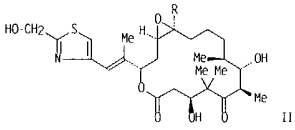
PRIORITY APPLN. INFO.: DE 1996-19647580 A 19961118
DE 1997-19707506 A 19970225
EP 1997-951233 A3 19971118
WO 1997-EP6442 W 19971118

GRAPHIC IMAGE:

L5 ANSWER 108 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I



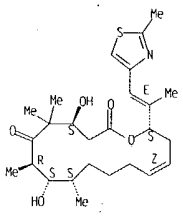
II

ABSTRACT:
The present invention concerns the epothilones, especially epothilone C [I; R = H] and epothilone D [I; R = Me] as well as epothilone E [II; R = H] and epothilone F [II; R = Me], the production process, and their application for producing therapeutic agents, including cytostatic agents as well as phytosanitary agents.

IT **186692-73-9P**, Epothilone C
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(epothilone C, D, E and F, production process, and use as cytostatics well as phytosanitary agents)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

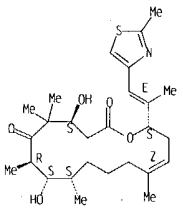
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 108 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **189453-10-9P**, Epothilone D
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(epothilone C, D, E and F, production process, and use as cytostatics well as phytosanitary agents)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

L5 ANSWER 108 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 109 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:163596 CAPLUS
DOCUMENT NUMBER: 128:217229
TITLE: Method for producing epothilones and the intermediate products obtained during the production process
INVENTOR(S): Schinzer, Dieter; Limberg, Anja; Bohm, Oliver M.; Bauer, Armin; Cordes, Martin
PATENT ASSIGNEE(S): Novartis Aktiengesellschaft, Switz.; Schinzer, Dieter; Limberg, Anja; Bohm, Oliver M.; Bauer, Armin; Cordes, Martin
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808849	A1	19980305	WO 1997-DE111	19970115 <--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19636343	C1	19971023	DE 1996-19636343	19960830 <--
DE 19645361	A1	19980430	DE 1996-19645361	19961028 <--
DE 19645362	A1	19980430	DE 1996-19645362	19961028 <--
AU 9721493	A1	19980319	AU 1997-21493	19970115 <--
AU 716610	B2	20000302		
EP 923583	A1	19990623	EP 1997-914077	19970115 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 334821	A	20001222	NZ 1997-334821	19970115 <--
JP 2001500851	T2	20010123	JP 1998-511141	19970115 <--

PRIORITY APPLN. INFO.: DE 1996-19636343 A 19960830
DE 1996-19645361 A 19961028
DE 1996-19645362 A 19961028
WO 1997-DE111 W 19970115
OTHER SOURCE(S): CASREACT 128:217229; MARPAT 128:217229
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

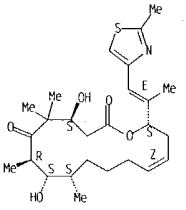
ABSTRACT:
A method for producing epothilones I [R = H (A), Me (B)] is characterized by

L5 ANSWER 109 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
reaction of thiazole II with carboxylic acid III (B = CH2Ph, THP, silyl protecting group; R = H, Me), followed by olefin metathesis in the presence of a noble metal catalyst, hydroxyl deprotection and epoxidn. Thus, epothilone A (I; R = H) was prepd. via acylation of II with III (R = H, B = SiMe2CMe3) in CH2Cl2 contg. DCC and DMAP, followed by olefin metathesis in CH2Cl2 contg. catalytic benzylidenebis(tricyclohexylphosphine)ruthenium dichloride, desilylation with aq. HF in Et2O/MeCN and epoxidn. with dimethyldioxirane in acetone. Epothilones A and B are natural substances which are produced by microorganisms and have similar properties to those of taxol and, therefore, are of interest to the pharmaceutical chem.

IT **186692-73-9P**, Epothilone C **189453-10-9P**,
Desoxyepothilone B **204194-92-3P 204195-20-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of epothilones via olefin metathesis)

RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

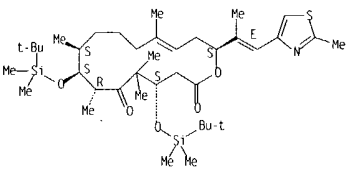
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

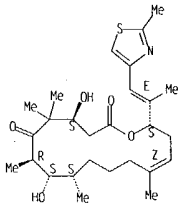
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 109 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



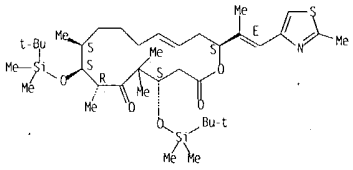
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 109 OF 131. CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204194-92-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4S-[4R*,7S*,8R*,9R*,16R*(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

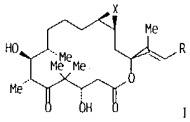


RN 204195-20-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.

L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:150476 CAPLUS
DOCUMENT NUMBER: 128:230166
TITLE: Total synthesis of epothilone E and analogs with modified side chains through the Stille coupling reaction
AUTHOR(S): Nicolaou, K. C.; He, Yun; Roschangar, Frank; King, N. Paul; Vourloumis, Dionisios; Li, Tianhu
CORPORATE SOURCE: Department of Chemistry, Skaggs Inst. for Chemical Biology, Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: Angewandte Chemie, International Edition (1998), 37(1/2), 84-87
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:230166
GRAPHIC IMAGE:



I

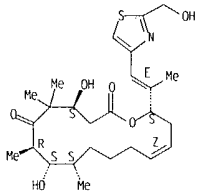
ABSTRACT:
The first total synthesis of epothilone E [I; R = 2-(hydroxymethyl)thiazol-4-yl, X = O] in which an olefin metathesis is used to form the macrocyclic lactone and a Stille coupling reaction is used to form the side chain is reported. The Stille coupling reaction was used to prepare deoxygenated side-chain analogs I [R = thiazol-4-yl, thiazol-5-yl, thiazol-2-yl, 2-(5-acetoxypentyl)thiazol-4-yl, 2-piperidinothiazol-4-yl, 2-(methylthio)thiazol-4-yl, 2-furyl, 2-thienyl, Ph, 3-pyridyl; X = bond].

IT **204513-12-2P**, Desoxyepothilone E **204513-16-6P**
204513-26-8P 204513-28-0P 204513-30-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of epothilone E and analogs through the Stille coupling reaction)

RN 204513-12-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

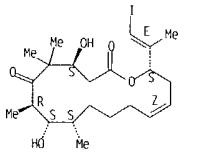
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-16-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

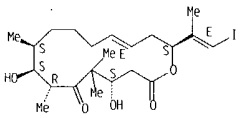
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 204513-26-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

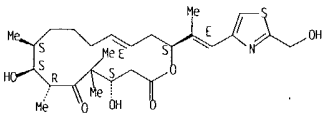
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **204513-14-4P 204513-35-9P 204513-36-0P**
204513-37-1P 204513-38-2P 204513-39-3P
204513-40-6P 204513-41-7P 204513-42-8P
204513-43-9P 204513-44-0P 204513-45-1P
204513-46-2P 204513-47-3P 204513-48-4P
204513-49-5P 204513-50-8P 204513-51-9P
204513-52-0P 204513-53-1P 204513-54-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of epothilone E and analogs through the Stille coupling reaction)
RN 204513-14-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-[2-(hydroxymethyl)-4-thiazolyl]-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

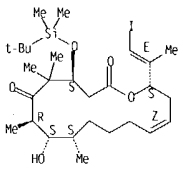
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

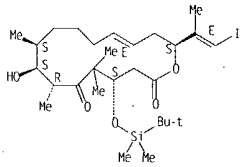
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-28-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

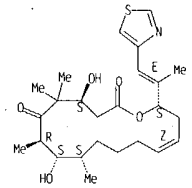
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-30-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-16-[(1E)-2-iodo-1-methylethenyl]-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

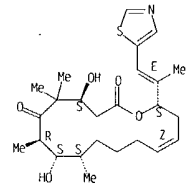
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-36-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

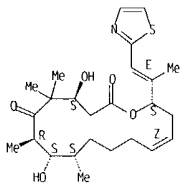
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-37-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

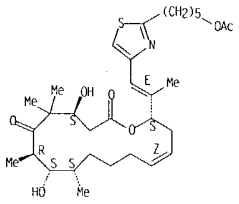
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-38-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[5-(acetyloxy)pentyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

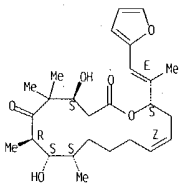
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-39-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(1-piperidinyl)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

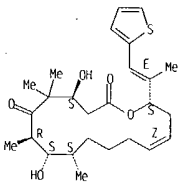
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-42-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

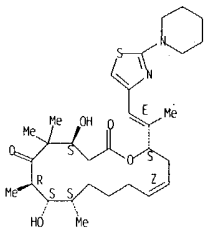
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-43-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

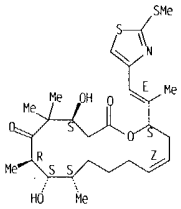
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 204513-40-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

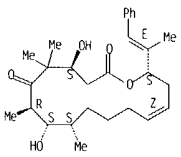
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-41-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

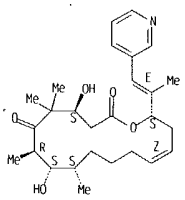
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



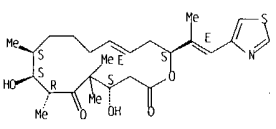
RN 204513-44-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



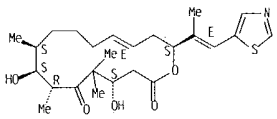
RN 204513-45-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



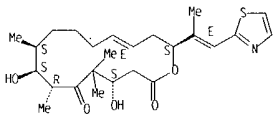
L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 204513-46-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(5-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-47-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

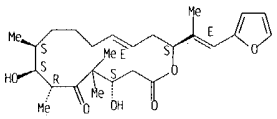


RN 204513-48-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-[2-[5-(acetyloxy)pentyl]-4-thiazolyl]-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

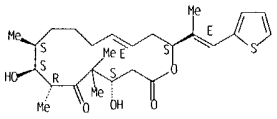
L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



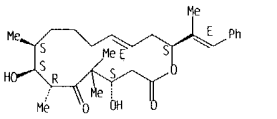
RN 204513-52-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-thienyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



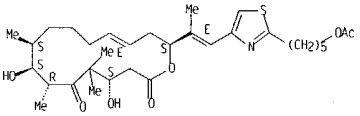
RN 204513-53-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



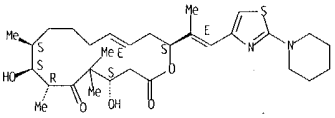
RN 204513-54-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(3-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA

L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



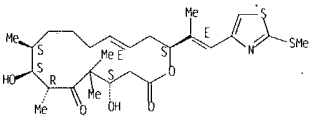
RN 204513-49-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(1-piperidinyl)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-50-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[2-(methylthio)-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

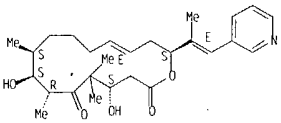
Absolute stereochemistry.
Double bond geometry as shown.



RN 204513-51-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 16-[(1E)-2-(2-furanyl)-1-methylethenyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA

L5 ANSWER 110 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



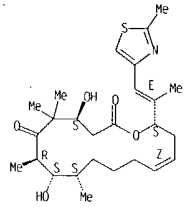
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 111 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:121923 CAPLUS
DOCUMENT NUMBER: 128:252599
TITLE: Farnesyl transferase inhibitors cause enhanced mitotic sensitivity to taxol and epothilones
AUTHOR(S): Moasser, Mark M.; Sepp-Lorenzino, Laura; Kohl, Nancy E.; Oliff, Allen; Balog, Aaron; Su, Dai-Shi; Danishefsky, Samuel J.; Rosen, Neal
CORPORATE SOURCE: Department of Medicine, Memorial Sloan-Kettering Cancer Center, Sloan-Kettering Institute, New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(4), 1369-1374
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
An important class of cellular proteins, which includes members of the p21ras family, undergoes post-translational farnesylation, a modification required for their partition to membranes. Specific farnesyl transferase inhibitors (FTIs) have been developed that selectively inhibit the processing of these proteins. FTIs have been shown to be potent inhibitors of tumor cell growth in cell culture and in murine models and at doses that cause little toxicity to the animal. These data suggest that these drugs might be useful therapeutic agents. We now report that, when FTI is combined with some cytotoxic antineoplastic drugs, the effects on tumor cells are additive. No interference is noted. Furthermore, FTI and agents that prevent microtubule depolymn., such as taxol or epothilones, act synergistically to inhibit cell growth. FTI causes increased sensitivity to induction of metaphase block by these agents, suggesting that a farnesylated protein may regulate the mitotic check point. The findings imply that FTI may be a useful agent for the treatment of tumors with wild-type ras that are sensitive to taxanes.

RT 186692-73-9, Desoxyepothilone A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(farnesyl transferase inhibitors cause enhanced mitotic sensitivity to taxol and epothilones)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

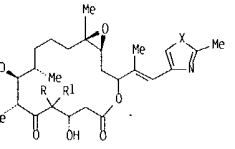
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 111 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 112 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:50907 CAPLUS
DOCUMENT NUMBER: 128:180246
TITLE: Total synthesis of oxazole- and cyclopropane-containing epothilone B analogs by the macrolactonization approach
AUTHOR(S): Nicolaou, K. C.; Sarabia, Francisco; Finlay, M. Ray V.; Ninkovic, Sacha; King, N. Paul; Vourloumis, Dionisios; He, Yun
CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Chemistry--A European Journal (1997), 3(12), 1971-1986
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:



I

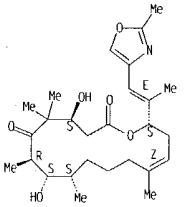
ABSTRACT:
In order to probe structure-activity relationships in the epothilone area, two series of epothilone B analogs were designed and synthesized. The first series contaiing an oxazole moiety in place of a thiazole on the side chain was constructed via utilization of key intermediates whereas the second series contaiing an ethano group instead of the gem-di-Me group at position 4 was synthesized. A Yamaguchi-type macrolactonization reaction was used to construct the macrocycle from a secoacid, which was assembled, in both cases, via a) an aldol reaction, b) an Enders alkylation, and c) a Wittig-type reaction. This convergent strategy provided access to oxazole and 4,4-ethano analogs, e.g., I (R = R1 = Me, X = O, S; RR1 = CH2CH2, X = O, S).

RT 198571-09-4P 198571-11-8P 203252-73-7P
203252-74-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of oxazole- and cyclopropane-containing epothilone B analogs via macrolactonization)

L5 ANSWER 112 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

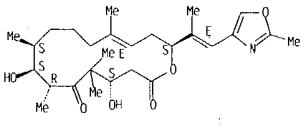
RN 198571-09-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-11-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

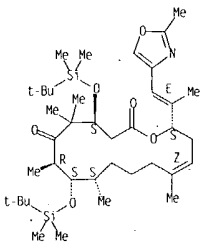
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 203252-73-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

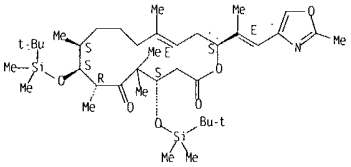
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 112 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



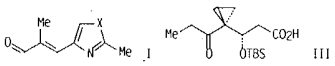
RN 203252-74-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 113 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:50906 CAPLUS
DOCUMENT NUMBER: 128:140541
TITLE: Total synthesis of oxazole- and cyclopropane-containing epothilone A analogs by the olefin metathesis approach
AUTHOR(S): Nicolaou, K. C.; Vallberg, Hans; King, N. Paul; Roschangar, Frank; He, Yun; Vourloumis, Dionisios; Nicolaou, Christopher G.
CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Chemistry--A European Journal (1997), 3(12), 1957-1970
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:

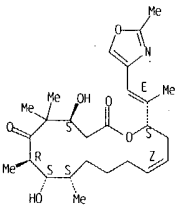


ABSTRACT:
For structure-activity relationship studies, two series of epothilone A analogs have been designed and synthesized, one containing an oxazole moiety instead of the thiazole heterocycle and the other containing a spirocyclopropane moiety in place of the gem-di-Me group at position C-4 (4,4-ethano-epothilones). The olefin metathesis strategy in solution was utilized for the chemical synthesis of these compds. starting with key building blocks (I) (X = O), (S)-H2C=CH(CH2)3CH(Me)CHO (II), (S)-MeCH2COCMe2CH(OSiMe2CMe3)CH2CO2H for the oxazole series and building blocks I (X = S), II, and (III) for the 4,4-ethano series. The convergent strategy towards the designed epothilone A series involved: a- an aldol condensation reaction, b- an esterification reaction, c- an olefin metathesis reaction catalyzed by [RuCl2(=CHPh)-(PCy3)2], and d- epoxidn. of the macrocycle double bond.

IT **198475-12-6P 198571-10-7P 198571-15-2P**
198571-19-6P 202333-40-2P 202333-45-7P
202333-46-8P 202333-47-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of oxazole- and cyclopropane-containing epothilone A

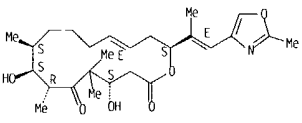
L5 ANSWER 113 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
analogs by the olefin metathesis approach)
RN 198475-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-10-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

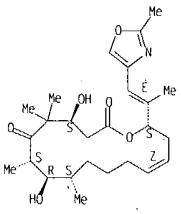
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-15-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)- (9CI) (CA INDEX NAME)

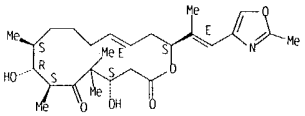
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 113 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-19-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)- (9CI) (CA INDEX NAME)

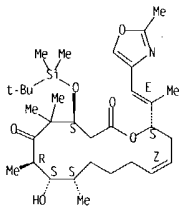
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 202333-40-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

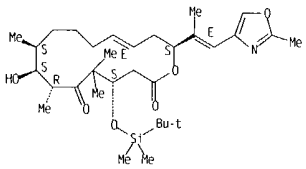
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 113 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 202333-45-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

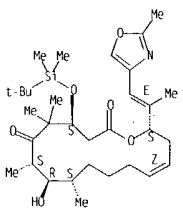
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 202333-46-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, [4S-[4R*,7R*,8S*,9R*,13Z,16R*(E)]]- (9CI) (CA INDEX NAME)

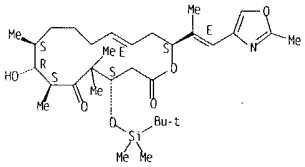
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 113 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 202333-47-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, [4S-[4R*,7R*,8S*,9R*,13E,16R*(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



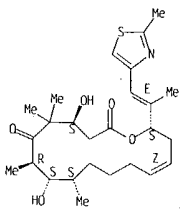
REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 114 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:729 CAPLUS
DOCUMENT NUMBER: 128:88685
TITLE: Metathesis vs metastasis: the chemistry and biology of the epothilones
AUTHOR(S): Finlay, Ray
CORPORATE SOURCE: Dep. Chemistry, The Skaggs Inst. for Chemical Biol., The Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: Chemistry & Industry (London) (1997), (24), 991-996
CODEN: CHINAG; ISSN: 0009-3068
PUBLISHER: Society of Chemical Industry
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ABSTRACT:
A review with 15 refs. on a recent entry onto the scene of potentially useful natural products, the epothilones A - E, providing valuable information for the fight against cancer via their interaction with microtubules.

IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(chemical and bioactivity of the epothilones)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

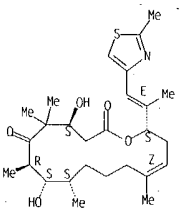
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 114 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

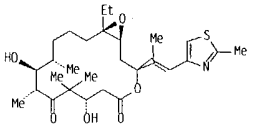
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 115 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:787450 CAPLUS
DOCUMENT NUMBER: 128:101936
TITLE: Total synthesis of 26-hydroxyepothilone B and related analogs
AUTHOR(S): Nicolaou, K. C.; Ninkovic, Sacha; Finlay, M. Ray V.; Sarabia, Francisco; Li, Tianhu
CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of California, California, 92093, USA
SOURCE: Chemical Communications (Cambridge) (1997), (24), 2343-2344
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:101936
GRAPHIC IMAGE:



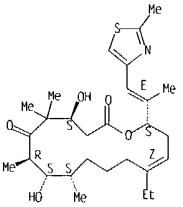
I

ABSTRACT:
A series of 26-substituted epothilones B, e.g. I, were constructed by total synthesis involving a selective Wittig olefination, an aldol reaction and a macrolactonization as key steps.

IT **198475-04-6P 201136-91-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of 26-hydroxyepothilone B and related analogs)
RN 198475-04-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

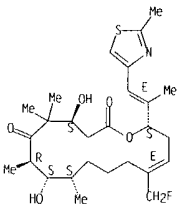
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 115 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



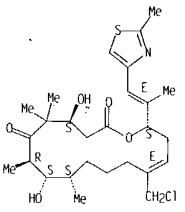
RN 201136-91-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(fluoromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



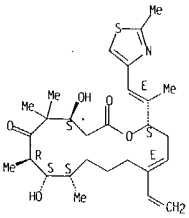
IT **201136-88-1P 201136-92-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(total synthesis of 26-hydroxyepothilone B and related analogs)
RN 201136-88-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(chloromethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 115 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



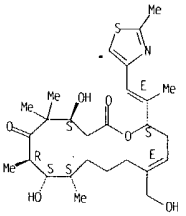
RN 201136-92-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethenyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



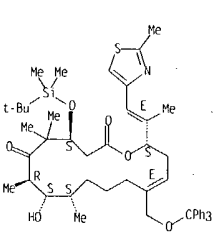
IT **201136-64-3P 201136-78-9P 201136-85-8P**
201136-86-9P 201136-89-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of 26-hydroxyepothilone B and related analogs)
RN 201136-64-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 115 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-78-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-[(triphenylmethoxy)methyl]-, [4S-[4R*,7S*,8R*,9R*,13E,16R*(E)]]- (9CI) (CA INDEX NAME)

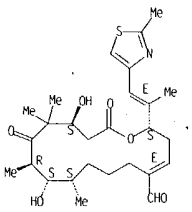
Absolute stereochemistry.
Double bond geometry as shown.



RN 201136-85-8 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxaldehyde, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

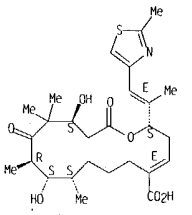
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 115 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-86-9 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxylic acid, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

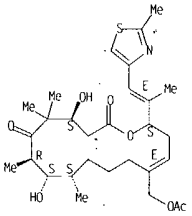


RN 201136-89-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-13-(methoxymethyl)-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

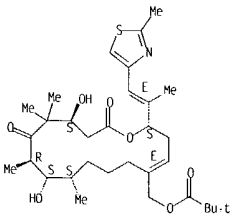
L5 ANSWER 115 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-83-6 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, [(2S,4E,9S,10S,11R,14S)-10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxooxacyclohexadec-4-en-5-yl]methyl ester (9CI) (CA INDEX NAME)

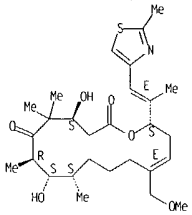
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-84-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-[(benzoyloxy)methyl]-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

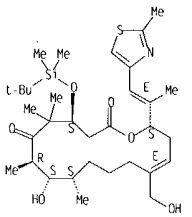
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 115 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



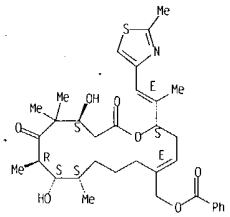
IT **201136-79-0P 201136-81-4P 201136-83-6P**
201136-84-7P 201136-87-0P 201136-90-5P
201136-93-8P 201136-94-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of 26-hydroxyepothilone B and related analogs)
RN 201136-79-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-13-(hydroxymethyl)-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4S-[4R*,7S*,8R*,9R*,13E,16R*(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



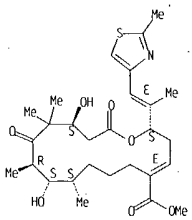
RN 201136-81-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-[(acetyloxy)methyl]-4,8-dihydroxy-

L5 ANSWER 115 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-87-0 CAPLUS
CN Oxacyclohexadec-4-ene-5-carboxylic acid, 10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxo-, methyl ester, (2S,4E,9S,10S,11R,14S)- (9CI) (CA INDEX NAME)

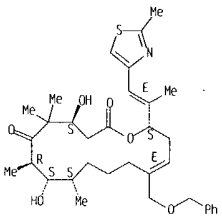
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-90-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-[(phenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

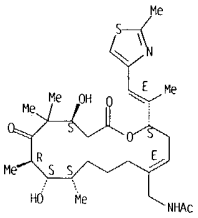
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 115 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 201136-93-8 CAPLUS
CN Acetamide, N-[[(2S,4E,9S,10S,11R,14S)-10,14-dihydroxy-9,11,13,13-tetramethyl-2-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-12,16-dioxooxacyclohexadec-4-en-5-yl]methyl]- (9CI) (CA INDEX NAME)

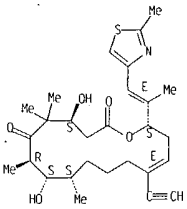
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 201136-94-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethynyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 115 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



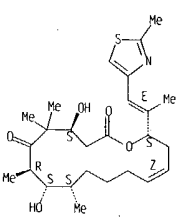
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 116 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:724919 CAPLUS
DOCUMENT NUMBER: 127:346221
TITLE: Synthesis of epothilones A and B in solid and solution phase. [Erratum to document cited in CA127:4950]
AUTHOR(S): Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Ninkovic, S.; Sarabia, F.; He, Y.; Vourloumis, D.; Yang, Z.; Li, T.; Giannakakou, P.; Hamel, E.
CORPORATE SOURCE: Dep. Chemistry, Skaggs Inst. Chem. Biology, Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: Nature (London) (1997), 390(6655), 100
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
Reference 19, includes, in addition to a total synthesis of epothilone B, biol. data for compound 23 and other congeners similar to the reported in the Letter.

IT **186692-73-9P 189453-10-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a combinatorial library via solid-phase synthesis of epothilone A and solution-phase synthesis of epothilone B (Erratum))
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

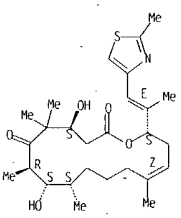
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

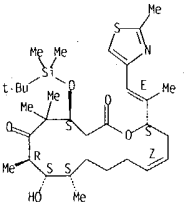
L5 ANSWER 116 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **187283-49-4P 187283-52-9P 188260-10-8P**
189453-35-8P 189453-40-5P 190369-82-5P
190369-85-8P 190370-08-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a combinatorial library via solid-phase synthesis of epothilone A and solution-phase synthesis of epothilone B (Erratum))
RN 187283-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

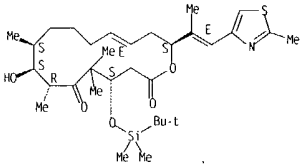
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 187283-52-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy

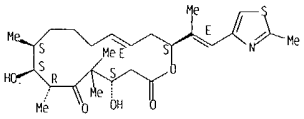
L5 ANSWER 116 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
]-8-hydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)-(9CI) (CA INDEX NAME)

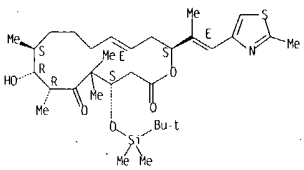
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-bis[[(1.1-dimethylethyl)dimethylsilyl]oxy]-5.5.7.9.13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13Z.16S)- (9CI) (CA INDEX NAME)

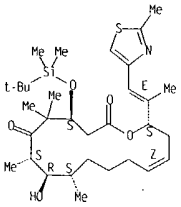
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 116 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 190369-85-8 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4-[[(1.1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5.5.7.9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. [4S-[4R*.7R*.8S*.9R*.13Z.16R*(E)]]- (9CI) (CA INDEX NAME)

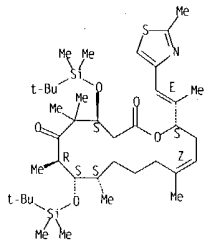
Absolute stereochemistry.
Double bond geometry as shown.



RN 190370-08-2 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-bis[[(1.1-dimethylethyl)dimethylsilyl]oxy]-5.5.7.9.13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

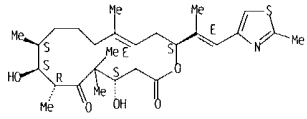
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 116 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9.13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)-(9CI) (CA INDEX NAME)

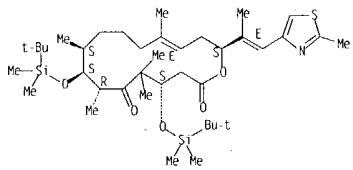
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 190369-82-5 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4-[[(1.1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5.5.7.9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. [4S-[4R*.7S*.8S*.9R*.13E.16R*(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 116 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:714315 CAPLUS
DOCUMENT NUMBER: 128:3560
TITLE: Designed epothilones: combinatorial synthesis, tubulin assembly properties, and cytotoxic action against taxol-resistant tumor cells
AUTHOR(S): Nicolaou, K. C.; Vourloumis, Dionisios; Li, Tianhu; Pastor, Joaquin; Winssinger, Nicolas; He, Yun; Ninkovic, Sacha; Sarabia, Francisco; Vallberg, Hans; Roschangar, Frank; King, N. Paul; Finlay, M. Ray V.; Giannakakou, Pareskevi; Verdier-Pinard, Pascal; Hamel, Ernest
CORPORATE SOURCE: Department of Chemistry and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Angewandte Chemie, International Edition in English (1997), 36(19), 2097-2103
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: Wiley-VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The title work demonstrates the power of interfacing combinatorial chemical with chemical biol. as facilitated by solid-phase synthesis, radiofrequency encoded combinatorial chemical and modern biol. assays. A library of 112 epothilones were prepared by solid-phase synthesis, their structure activity relationships measured by tubulin binding assay and some tested for inhibition of carcinoma cell growth.

IT **186692-73-9P 188259-95-2P 188260-10-8P**
188260-34-6P 189453-10-9P 189453-40-5P
192370-82-4P 193071-86-2P 193146-35-9P
198475-12-6P 198571-04-9P 198571-09-4P
198571-10-7P 198571-11-8P 198571-15-2P
198571-16-3P 198571-17-4P 198571-18-5P
198571-19-6P 198571-20-9P 198571-21-0P
198571-22-1P 198571-24-3P 198571-25-4P
198571-26-5P 198571-28-7P 198571-29-8P
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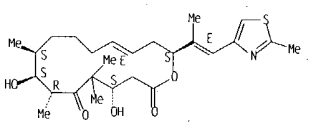
198571-68-5P 198571-69-6P 198571-70-9P
198571-71-0P 198571-72-1P 198571-73-2P
198571-74-3P 198571-76-5P 198571-77-6P
198571-78-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

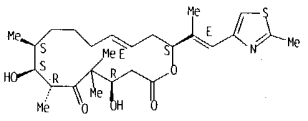
L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-34-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

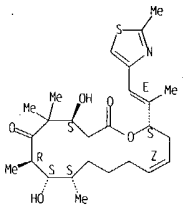


RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

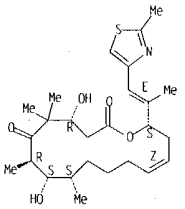
L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(combinatorial synthesis of epothilone library, tubulin assembly properties, and cytotoxic action against taxol-resistant tumor cells)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

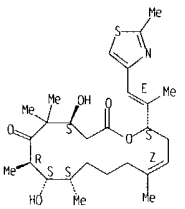


RN 188259-95-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

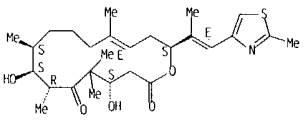


L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

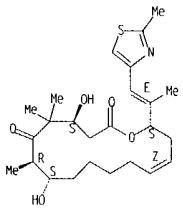
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 192370-82-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

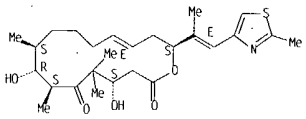
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 193071-86-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

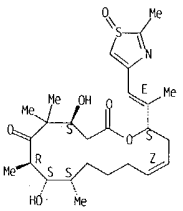
Absolute stereochemistry.
Double bond geometry as shown.



RN 193146-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

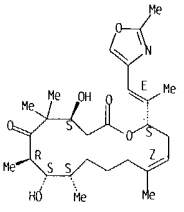
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-09-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

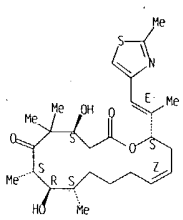
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-10-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

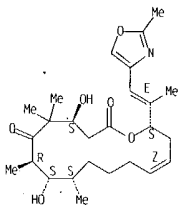
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



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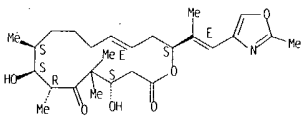
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-1-oxido-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

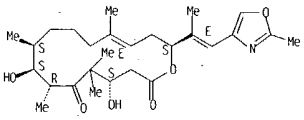
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



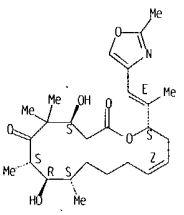
RN 198571-11-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-15-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

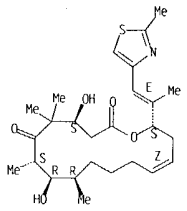
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-16-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-

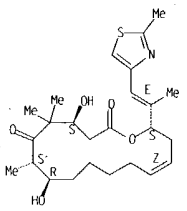
L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S,7S,8R,9R,13Z,16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



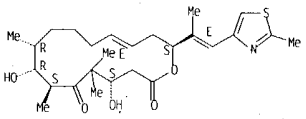
RN 198571-17-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



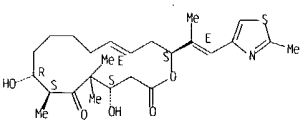
RN 198571-18-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8S,13Z,16S)-
(9CI) (CA INDEX NAME)

L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-21-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-22-1 CAPLUS
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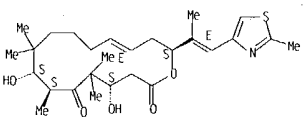
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

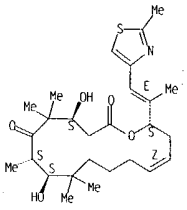


RN 198571-24-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8R,13Z,16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

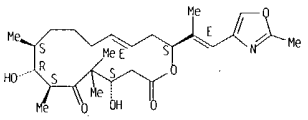
L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-19-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-
(9CI) (CA INDEX NAME)

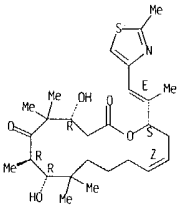
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198571-20-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9R,13E,16S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-25-4 CAPLUS
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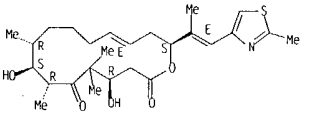
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-26-5 CAPLUS
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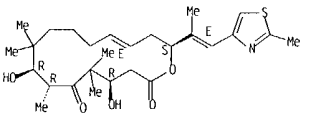
(9CI) (CA INDEX NAME)

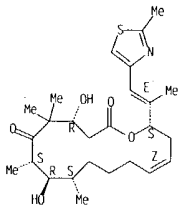
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-28-7 CAPLUS

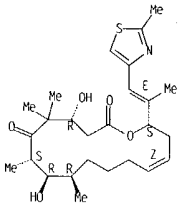
L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-29-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9R,13Z,16S)-(9CI) (CA INDEX NAME)

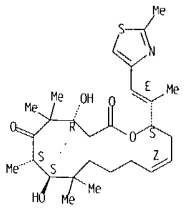
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-30-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8S,13Z,16S)-

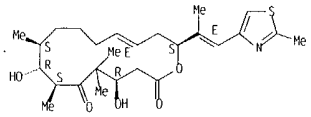
L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-31-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

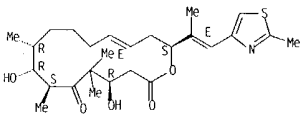
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-32-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8R,9R,13E,16S)-(9CI) (CA INDEX NAME)

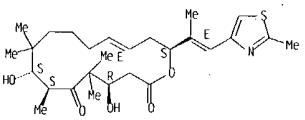
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



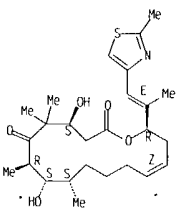
RN 198571-33-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7S,8S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-37-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16R)-(9CI) (CA INDEX NAME)

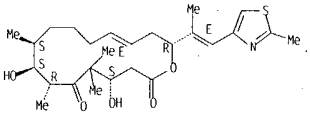
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-38-9 CAPLUS

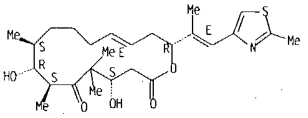
L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



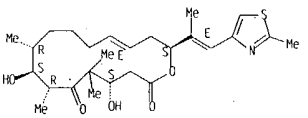
RN 198571-39-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-66-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13E,16S)-(9CI) (CA INDEX NAME)

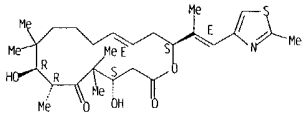
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-67-4 CAPLUS

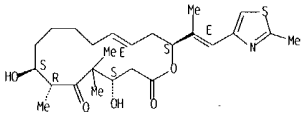
L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazoiyl)ethenyl]-, (4S,7R,8R,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-68-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13E,16S)- (9CI) (CA INDEX NAME)

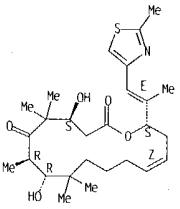
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-69-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-[(2-methyl-4-thiazolyl)methylene]propyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

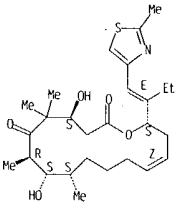
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-72-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-[(2-methyl-4-thiazolyl)methylene]propyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

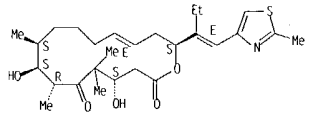
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-73-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

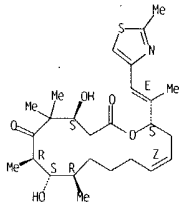
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198571-70-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9R,13Z,16S)-(9CI) (CA INDEX NAME)

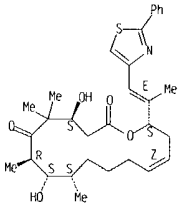
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-71-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,9-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8R,13Z,16S)-(9CI) (CA INDEX NAME)

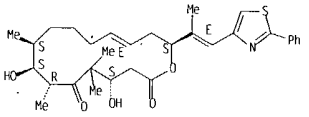
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



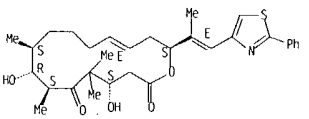
RN 198571-74-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-76-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-phenyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

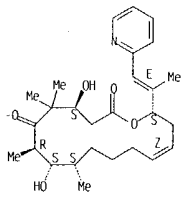
Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-77-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-

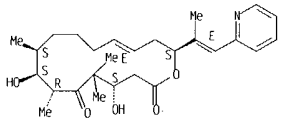
L5 ANSWER 117 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 198571-78-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-pyridinyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

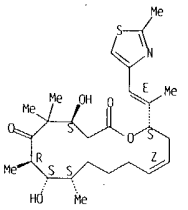
L5 ANSWER 118 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:714314 CAPLUS
DOCUMENT NUMBER: 127:358730
TITLE: Structure-activity relationships of the epothilones and the first in vivo comparison with paclitaxel
AUTHOR(S): Su, Dai-Shi; Balog, Aaron; Meng, Dongfang; Bertinato, Peter; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.
CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Angewandte Chemie, International Edition in English (1997), 36(19), 2093-2096
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: Wiley-VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
ABSTRACT:
The structure-activity relationships of the epothilones and 18 derivs. and analogs were studied. An in vivo comparison of the chemotherapeutic effect of epothilone B with that of paclitaxel was also studied. The chemotherapeutic effect of daily doses of epothilone B (0.7 mg/kg) and paclitaxel (2 mg/kg) in CB-17 SCID mice bearing drug-resistant human CCRF-CEM/VBL xenografts were T/C = 0.33 and T/C = 0.70, resp.

IT **186692-73-9**, Desoxyepothilone A **188260-10-8**
189453-10-9, Desoxyepothilone B **189453-40-5**
198475-04-6 **198475-05-7** **198475-06-8**
198475-07-9 **198475-11-5** **198475-12-6**
198475-13-7 **198475-18-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(structure-activity relationships of the epothilones and in vivo comparison with paclitaxel)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

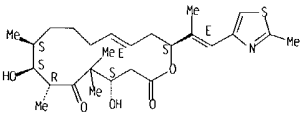
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 118 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

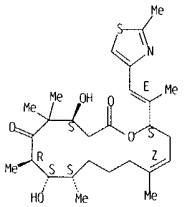
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

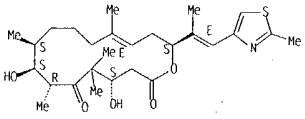
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 118 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

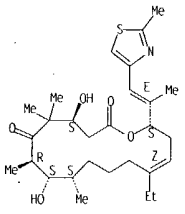
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198475-04-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

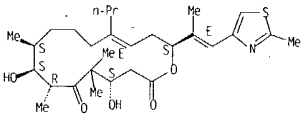
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 118 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-05-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

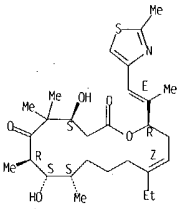
Absolute stereochemistry.
Double bond geometry as shown.



RN 198475-06-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-propyl-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

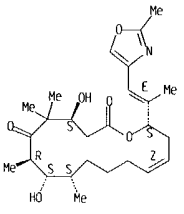
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 118 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-12-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-oxazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

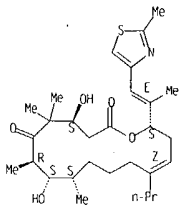
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 198475-13-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-phenylethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

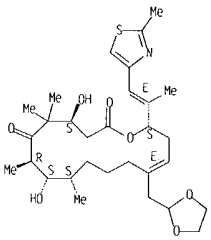
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 118 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-07-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-(1,3-dioxolan-2-ylmethyl)-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

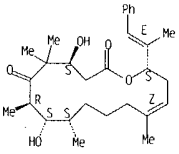
Absolute stereochemistry: Rotation (-).
Double bond geometry as shown.



RN 198475-11-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-ethyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16R)- (9CI) (CA INDEX NAME)

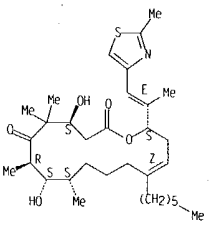
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 118 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 198475-18-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 13-hexyl-4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

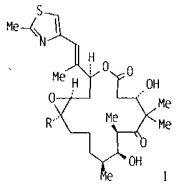
Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 119 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:665094 CAPLUS
DOCUMENT NUMBER: 127:293040
TITLE: Total Syntheses of Epothilones A and B
AUTHOR(S): Meng, Dongfang; Bertinato, Peter; Balog, Aaron; Su, Dai-Shi; Kamenecka, Ted; Sorensen, Erik; Danishefsky, Samuel J.
CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Journal of the American Chemical Society (1997), 119(42), 10073-10092
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:293040
GRAPHIC IMAGE:



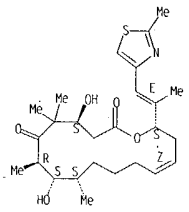
I

ABSTRACT:
Convergent, stereocontrolled total syntheses of the microtubule-stabilizing macrolides epothilones A (I; R = H) and B (I; R = Me) have been achieved. Four distinct ring-forming strategies were pursued. Of these four, three were reduced to practice. In one approach, the action of a base on a substance possessing an acetate ester and a nonenolizable aldehyde brought about a remarkably effective macroaldolization simultaneously creating the C2-C3 bond and the hydroxyl-bearing stereocenter at C-3. Alternatively, the 16-membered macrolide of the epothilones could be fashioned through a C12-C13 ring-closing olefin metathesis and through macrolactonization of the appropriate hydroxy acid. The application of a stereospecific B-alkyl Suzuki coupling strategy permitted the establishment of a cis C12-C13 olefin, thus setting the stage for an eventual site- and diastereoselective epoxidn. reaction. The development of a novel cyclopropane solvolysis strategy for incorporating the geminal Me groups of the epothilones, and the use of Lewis acid catalyzed diene-aldehyde cyclocondensation (LACDAC) and asym. allylation methodol. are also noteworthy.

IT **186692-73-9P**, (-)-Desoxyepothilone A **186692-84-2P**
188259-95-2P, 3-epi-Desoxyepothilone A **188260-22-2P**
189453-10-9P, (-)-Desoxyepothilone B **189453-35-8P**
190370-08-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(syntheses of epothilones A and B via macroaldolization, olefin metathesis and macrolactonization)

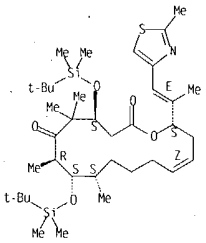
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



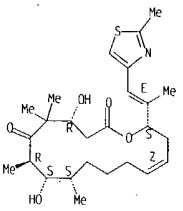
RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



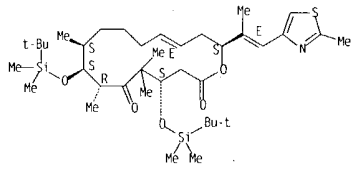
RN 188259-95-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



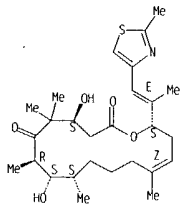
RN 188260-22-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

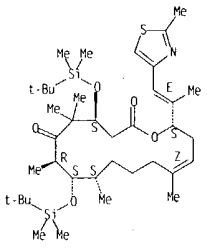
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

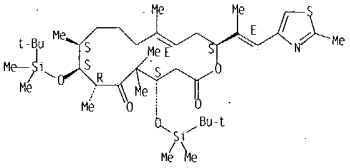
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 119 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



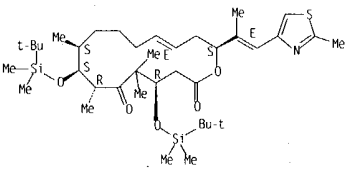
RN 190370-08-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



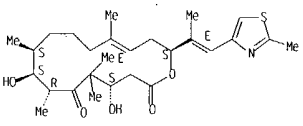
IT **188259-92-9P 188260-10-8P 188260-30-2P**
189453-40-5P, (E)-Desoxyepothilone B
RL: SPN (Synthetic preparation); PREP (Preparation)
(syntheses of epothilones A and B via macroaldolization, olefin metathesis and macrolactonization)
RN 188259-92-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-

L5 ANSWER 119 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



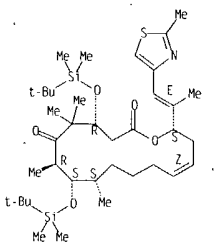
RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



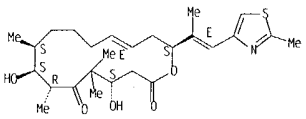
L5 ANSWER 119 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
methyl-4-thiazolyl)ethenyl]-, [4R-[4R*,7R*,8S*,9S*,13Z,16S*(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-30-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4R-[4R*,7R*,8S*,9S*,13E,16S*(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L5 ANSWER 120 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1997:528753 CAPLUS
DOCUMENT NUMBER:	127:135660
TITLE:	Total Syntheses of Epothilones A and B via a Macrolactonization-Based Strategy
AUTHOR(S):	Nicolaou, K. C.; Ninkovic, S.; Sarabia, F.; Vourloumis, D.; He, Y.; Vallberg, H.; Finlay, M. R. V.; Yang, Z.
CORPORATE SOURCE:	Department of Chemistry and The Skaggs Institute for Chemical Biology, La Jolla, CA, 92037, USA
SOURCE:	Journal of the American Chemical Society (1997), 119(34), 7974-7991 CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 127:135660
GRAPHIC IMAGE:	

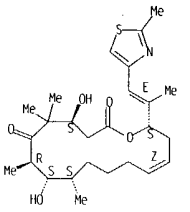
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
The total syntheses of epothilones A (I) (R = H) and B I (R = Me) and several analogs are described. The reported strategy relies on a macrolactonization approach and features selective epoxidn. of the macrocycle double bond in precursors II (R = H, Me) as well as high convergency and flexibility. Building blocks (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CO2H, (S)-Me3CMe2SiOCH2CH(Me)CH2CH2CH2COR (R = H, Me), (III) [R2 = CH2CH2P+(Ph)3I-; CH2CHO] were constructed by asym. processes and coupled via Wittig, aldol, and macrolactonization reactions to afford the basic skeleton of epothilones and that of several of their analogs by a relatively short route. The utilization of intermediate III [R2 = (E)-CH2CH=C(Me)CH2CH2CH2I], obtained via a stereoselective Wittig reaction and its Enders coupling to SAMP hydrazone, in combination with a stereoselective aldol reaction with the modified substrate (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CH2OSiMe2CMe3 improved the stereoselectivity and efficiency of the total synthesis of these new and highly potent microtubule binding antitumor agents.

IT **186692-73-9P 186692-84-2P 189453-10-9P**
189453-35-8P 189453-40-5P 190370-08-2P
193146-34-8P 193146-35-9P 193146-48-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total syntheses of epothilones A and B via a macrolactonization-based strategy)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

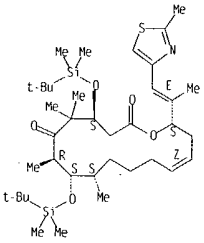
L5 ANSWER 120 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

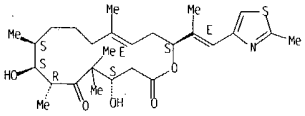
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-

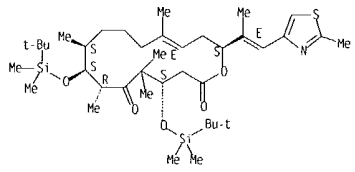
L5 ANSWER 120 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 190370-08-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

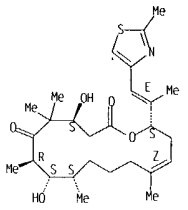


RN 193146-34-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

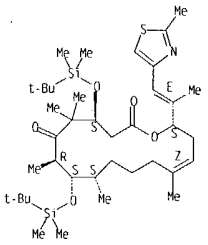
L5 ANSWER 120 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

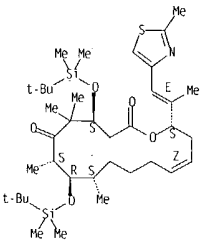


RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

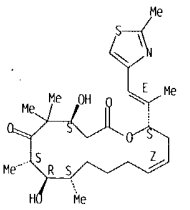


L5 ANSWER 120 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 193146-35-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13Z,16S)- (9CI) (CA INDEX NAME)

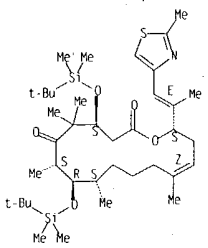
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 193146-48-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4S-[4R*,7R*,8S*,9R*,13Z,16R*(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 120 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



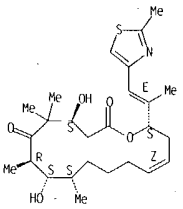
L5 ANSWER 121 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:528752 CAPLUS
DOCUMENT NUMBER: 127:149021
TITLE: The Olefin Metathesis Approach to Epothilone A and Its Analogs
AUTHOR(S): Nicolaou, K. C.; He, Y.; Vourloumis, D.; Vallberg, H.; Roschangar, F.; Sarabia, F.; S.Ninkovic; Yang, Z.; Trujillo, J. I.
CORPORATE SOURCE: Department of Chemistry and The Skaggs, Institute for Chemical Biology, La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (1997), 119(34), 7960-7973
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:149021
GRAPHIC IMAGE: For diagram(s), see printed CA Issue.
ABSTRACT:
The olefin metathesis approach to epothilone A (I) and several diastereomeric analogs is described. Key building blocks II, (S)-OHCCH(Me)CH2CH2CH2CH=CH2, and (S)-MeCH2COC(Me)2CH(OSiMe2CMe3)CH2CO2H were constructed in optically active form and were coupled and elaborated to olefin metathesis precursor III (R = SiMe2CMe3) via an aldol reaction and an esterification coupling. Olefin metathesis of compound III (R = SiMe2CMe3), under the catalytic influence of RuCl2(:CHPh)(PCy3)2, furnished cis- and trans-cyclic olefins IV (R = SiMe2CMe3). Epoxidn. of (Z)-IV (R = H) gave I and several analogs, whereas epoxidn. of (E)-IV (R = H) resulted in addnl. epothilones. Similar elaboration of isomeric as well as simpler intermediates resulted in yet another series of epothilone analogs and model systems.

IT **186692-73-9P 187283-49-4P 187283-52-9P**
188260-10-8P 193071-85-1P 193071-86-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilone A and analogs via olefin metathesis)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

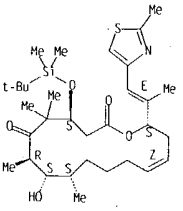
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 121 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 187283-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

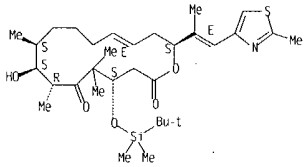
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 187283-52-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

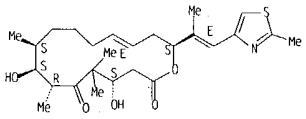
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 121 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

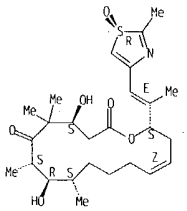
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 193071-85-1 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[(1R)-2-methyl-1-oxido-4-thiazolyl]ethenyl]-, (4S,7S,8R,9S,13Z,16S)- (9CI) (CA INDEX NAME)

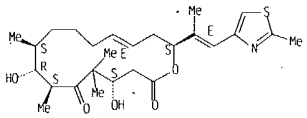
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 121 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 193071-86-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7S,8R,9S,13E,16S)-(9CI) (CA INDEX NAME)

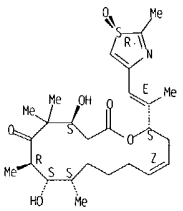
Absolute stereochemistry.
Double bond geometry as shown.



IT **193071-80-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of epothilone A and analogs via olefin metathesis)
RN 193071-80-6 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-[(1R)-2-methyl-1-oxido-4-thiazolyl]ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 121 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L5 ANSWER 122 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

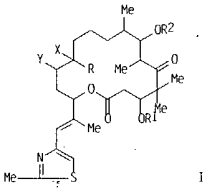
ACCESSION NUMBER: 1997:456769 CAPLUS
DOCUMENT NUMBER: 127:50474
TITLE: Preparation of epothilone derivatives as agrochemicals and pharmaceuticals
INVENTOR(S): Hoefle, Gerhard; Kiffe, Michael
PATENT ASSIGNEE(S): Gesellschaft fuer Biotechnologische Forschung Mbh (Gbf), Germany
SOURCE: Ger. Offen., 9 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 19542986	A1	19970522	DE 1995-19542986	19951117	<--
WO 9719086	A1	19970529	WO 1996-EP5080	19961118	<--
W: JP, US					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 873341	A1	19981028	EP 1996-939097	19961118	<--
EP 873341	B1	20030910			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
EP 903348	A1	19990324	EP 1998-121523	19961118	<--
EP 903348	B1	20020605			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2000500757	T2	20000125	JP 1997-519381	19961118	<--
EP 1186606	A1	20020313	EP 2001-127352	19961118	
EP 1186606	B1	20040317			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AT 218556	E	20020615	AT 1998-121523	19961118	
PT 903348	T	20021129	PT 1998-121523	19961118	
ES 2178093	T3	20021216	ES 1998-121523	19961118	
AT 249463	E	20030915	AT 1996-939097	19961118	
PT 873341	T	20040227	PT 1996-939097	19961118	
US 6288237	B1	20010911	US 1998-77055	19980803	<--
US 2001034452	A1	20011025	US 2001-836134	20010416	<--
US 6613912	B2	20030902			
US 2004087634	A1	20040506	US 2003-602770	20030625	

PRIORITY APPLN. INFO.:
DE 1995-19542986 A 19951117
DE 1996-19639456 A 19960925
EP 1996-939097 A3 19961118
WO 1996-EP5080 W 19961118
US 1998-77055 A3 19980803
US 2001-836134 A3 20010416

OTHER SOURCE(S): MARPAT 127:50474
GRAPHIC IMAGE:

L5 ANSWER 122 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



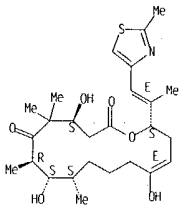
I

ABSTRACT:
The title compds., e.g., I [R = H, C1-4 alkyl; R1, R2 = H, C1-6 alkyl, C1-6 acyl, benzoyl, C1-4 trialkylsilyl, benzyl, Ph, C1-6 alkoxy, C6 alkyl-, hydroxy-, and halo-substituted benzyl or phenyl; X, Y = halo, OH, acyloxy, alkoxy, benzoyloxy], useful as agrochems. and pharmaceuticals (no data), are prepared Thus, epothilone A in acetone containing trifluoroacetic acid was heated overnight at 50° and the reaction mixture was adjusted to pH 7 with 1 M phosphate buffer to give 2 isomers, each in 19% yield.

IT **191105-80-3P 191105-81-4P**
RL: AGR (Agricultural use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilone derivs. as agrochems. and pharmaceuticals)
RN 191105-80-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8,13-trihydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4R*,7S*,8R*,9R*,13E,16R*(E)]-(9CI) (CA INDEX NAME)

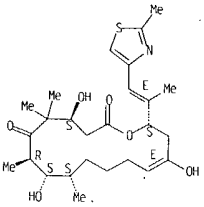
Relative stereochemistry.
Double bond geometry as shown.

L5 ANSWER 122 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 191105-81-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8,14-trihydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4R*,7S*,8R*,9R*,13E,16R*(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

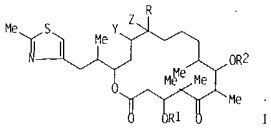


L5 ANSWER 123 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:443365 CAPLUS
DOCUMENT NUMBER: 127:81289
TITLE: Preparation of epothilone derivatives as agrochemicals and pharmaceuticals
INVENTOR(S): Hofle, Gerhard; Kiffe, Michael
PATENT ASSIGNEE(S): Gesellschaft Fur Biotechnologische Forschung Mbh (Gbf), Germany; Hofle, Gerhard; Kiffe, Michael
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719086	A1	19970529	WO 1996-EP5080	19961118 <--
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19542986	A1	19970522	DE 1995-19542986	19951117 <--
DE 19639456	A1	19980326	DE 1996-19639456	19960925 <--
EP 873341	A1	19981028	EP 1996-939097	19961118 <--
EP 873341	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000500757	T2	20000125	JP 1997-519381	19961118 <--
AT 249463	E	20030915	AT 1996-939097	19961118
US 6288237	B1	20010911	US 1998-77055	19980803 <--
US 2004087634	A1	20040506	US 2003-602770	20030625

PRIORITY APPLN. INFO.: DE 1995-19542986 A 19951117
DE 1996-19639456 A 19960925
WO 1996-EP5080 W 19961118
US 1998-77055 A3 19980803
US 2001-836134 A3 20010416

OTHER SOURCE(S): MARPAT 127:81289
GRAPHIC IMAGE:



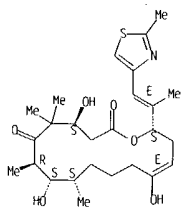
I

L5 ANSWER 123 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

ABSTRACT:
The title compds., e.g., I [R = H, C1-4 alkyl; R1, R2 = H, C1-6 alkyl, C1-6 acyl, benzoyl, C1-4 trialkylsilyl, benzyl, Ph, C1-6 alkoxy, C6 alkyl-, hydroxy-, and halo-substituted benzyl or phenyl; X, Y = H, halo, pseudohalo, OH, acyloxy, alkoxy, benzoyloxy; or YZ = O, bond; however, I may not be epothilone A or B], useful as agrochems. and pharmaceuticals (no data), are prepared Thus, epothilone A in acetone containing trifluoroacetic acid was heated overnight at 50° and the reaction mixture was adjusted to pH 7 with 1 M phosphate buffer to give 2 isomers, each in 19% yield.

IT **191105-80-3P 191105-81-4P**
RL: AGR (Agricultural use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of epothilone derivs. as agrochems. and pharmaceuticals)
RN 191105-80-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8,13-trihydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4R*,7S*,8R*,9R*,13E,16R*(E)]-(9CI) (CA INDEX NAME)

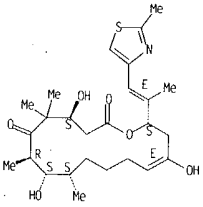
Relative stereochemistry.
Double bond geometry as shown.



RN 191105-81-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8,14-trihydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4R*,7S*,8R*,9R*,13E,16R*(E)]-(9CI) (CA INDEX NAME)

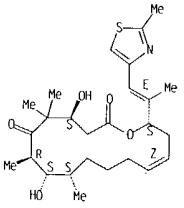
Relative stereochemistry.
Double bond geometry as shown.

L5 ANSWER 123 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **186692-73-9P**, Epothilone C **189453-10-9P**, Epothilone D
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of epothilone derivs. as agrochems. and pharmaceuticals)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

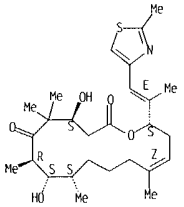
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 123 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



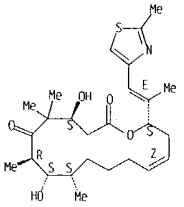
L5 ANSWER 124 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:430309 CAPLUS
DOCUMENT NUMBER: 127:108793
TITLE: Stereoselective syntheses and evaluation of compounds in the 8-desmethylepothilone A series: some surprising observations regarding their chemical and biological properties
AUTHOR(S): Balog, Aaron; Betinato, Peter; Su, Dai-Shi; Meng, Dongfang; Sorensen, Erik; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.
CORPORATE SOURCE: Lab. Bioorganic Chem., Sloan-Kettering Inst. Cancer Res., New York, NY, 10021, USA
SOURCE: Tetrahedron Letters (1997), 38(26), 4529-4532
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:108793
ABSTRACT:
The title compds. have been synthesized in a convergent way by recourse to a Weiler type dianion construction.

IT **186692-73-9**, Desoxyepothilone A **189453-10-9**, Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(stereoselective syntheses and evaluation of compds. in the 8-desmethylepothilone A series)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

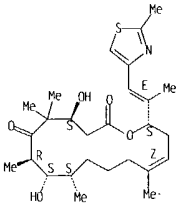
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 124 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

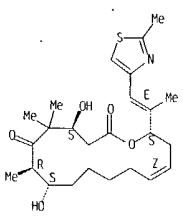
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **192370-82-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective syntheses and evaluation of compds. in the 8-desmethylepothilone A series)
RN 192370-82-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

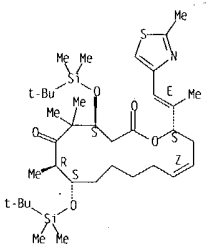
Absolute stereochemistry.

L5 ANSWER 124 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Double bond geometry as shown.



IT **192370-81-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereoselective syntheses and evaluation of compds. in the 8-desmethylepothilone A series)
RN 192370-81-3 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7-trimethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,13Z,16S)- (9CI) (CA INDEX NAME)

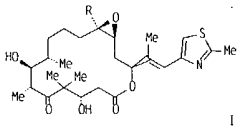
Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 125 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

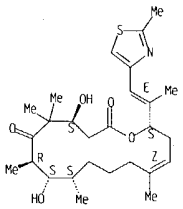
ACCESSION NUMBER: 1997:330310 CAPLUS
DOCUMENT NUMBER: 127:4950
TITLE: Synthesis of epothilones A and B in solid and solution phase
AUTHOR(S): Nicolaou, K. C.; Winssinger, N.; Pastor, J.; Ninkovic, S.; Sarabia, F.; He, Y.; Vourloumis, D.; Yang, Z.; Li, T.; Giannakakou, P.; Hamel, E.
CORPORATE SOURCE: Dep. Chemistry, Skaggs Inst. Chem. Biology, Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: Nature (London) (1997), 387(6630), 268-272
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:4950
GRAPHIC IMAGE:



I

ABSTRACT:
Epothilones A (I: R = H) and B (I: R = Me), two compds. that were recently isolated from myxobacterium Sorangium cellulosum strain 90, have generated intense interest among chemists, biologists and clinicians owing to the structural complexity, unusual mechanism of interaction with microtubules and anticancer potential of these mols. Like taxol, they exhibit cytotoxicity against tumor cells by inducing microtubule assembly and stabilization, even in taxol-resistant cell lines. Following the structural elucidation of these mols. by X-ray crystallog. in 1996, several synthesis of epothilones A and B have been reported, indicative of the potential importance of these mols. in the cancer field. Here we report the first solid-phase synthesis of epothilone A, the total synthesis of epothilone B, and the generation of a small epothilone library. The solid-phase synthesis applied here to epothilone A could open up new possibilities in natural-product synthesis and, together with solution-phase synthesis of other epothilones, paves the way for the generation of large combinatorial libraries of these important mols. for biol. screening.

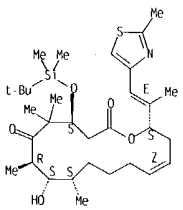
L5 ANSWER 125 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **187283-49-4P 187283-52-9P 188260-10-8P**
189453-35-8P 189453-40-5P 190369-82-5P
190369-85-8P 190370-08-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a combinatorial library via solid-phase synthesis of epothilone A and solution-phase synthesis of epothilone B)

RN 187283-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



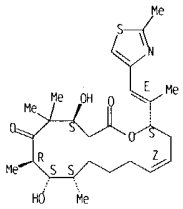
RN 187283-52-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

L5 ANSWER 125 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **186692-73-9P 189453-10-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a combinatorial library via solid-phase synthesis of epothilone A and solution-phase synthesis of epothilone B)

RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

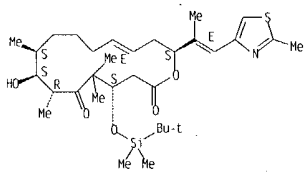
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

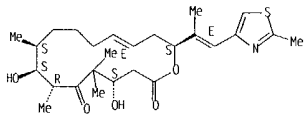
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 125 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

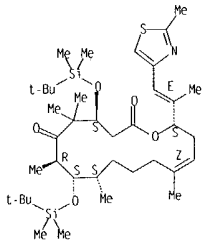
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

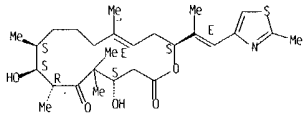
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 125 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

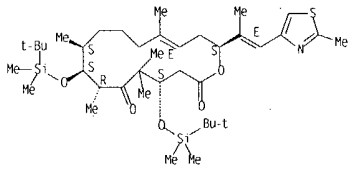
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 190369-82-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4S-[4R*,7S*,8S*,9R*,13E,16R*(E)]]- (9CI) (CA INDEX NAME)

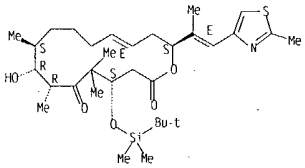
Absolute stereochemistry.
Double bond geometry as shown.

L5 ANSWER 125 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



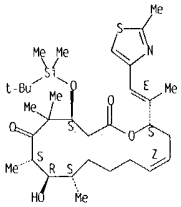
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 125 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 190369-85-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4S-[4R*,7R*,8S*,9R*,13Z,16R*(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 190370-08-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 126 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:302059 CAPLUS
DOCUMENT NUMBER: 127:4948
TITLE: Total synthesis of (-)-epothilone B: an extension of the Suzuki coupling method and insights into structure-activity relationships of the epothilones
AUTHOR(S): Su, Dai-Shi; Meng, Dongfang; Bertinato, Peter; Balog, Aaron; Sorensen, Erik J.; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.
CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Angewandte Chemie, International Edition in English (1997), 36(7), 757-759
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:4948
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

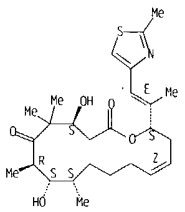
ABSTRACT:
(-)-Epothilone B (I: R = Me, X = O) and desoxyepothilone B (I: R = Me, X = bond) were prepared via Suzuki coupling of (Z)-vinyl iodide II with borane III. I (R = H, Me, X = O, bond) and the E-isomers of I (R = H, Me, X = bond) were tested for efficacy against drug-sensitive and resistant CCRF-CEM cell lines (IC50 = 0.0004 - 0.262 μM).

IT **186692-73-9**, Desoxyepothilone A **188260-10-8**, trans-Desoxyepothilone A **189453-40-5**, trans-Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis of epothilone B via a Suzuki coupling and insights into antitumor structure-activity relationships)

RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

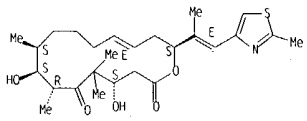
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 126 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

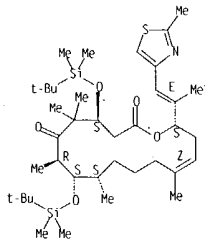


RN 189453-40-5 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

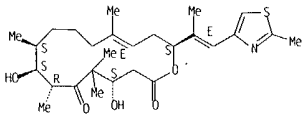
L5 ANSWER 126 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



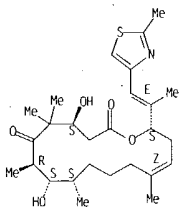
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 126 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT 189453-10-9P, Desoxyepothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilone B via a Suzuki coupling and insights into antitumor structure-activity relationships)
RN 189453-10-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

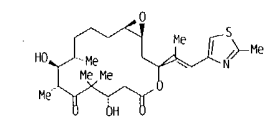
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



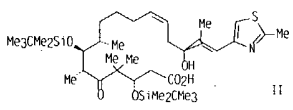
IT 189453-35-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of epothilone B via a Suzuki coupling and insights into antitumor structure-activity relationships)
RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-

L5 ANSWER 127 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1997:206419 CAPLUS
DOCUMENT NUMBER:	126:251010
TITLE:	Total synthesis of epothilone A: the macrolactonization approach
AUTHOR(S):	Nicolaou, K. C.; Sarabia, Francisco; Ninkovic, Sacha; Yang, Zhen
CORPORATE SOURCE:	Dep. Chem., Skaggs Inst. Chem. Biol., Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE:	Angewandte Chemie, International Edition in English (1997), 36(5), 525-527 CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER:	VCH
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 126:251010
GRAPHIC IMAGE:	



I

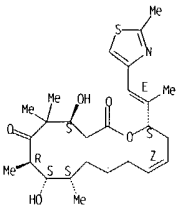


II

ABSTRACT:
Epothilone A (I) was prepared via a highly convergent and flexible route with macrolactonization of hydroxy acid II as the key step.

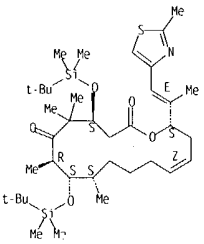
IT 186692-73-9P 186692-84-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of epothilone A via a macrolactonization approach)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

L5 ANSWER 127 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

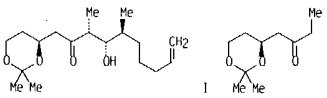
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 127 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L5 ANSWER 128 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:206418 CAPLUS
DOCUMENT NUMBER: 126:277316
TITLE: Total synthesis of (-)-epothilone A
AUTHOR(S): Schinzer, Dieter; Limberg, Anja; Bauer, Armin; Boehm, Oliver M.; Cordes, Martin
CORPORATE SOURCE: Dip. Chim., Inst. Org. Chem. Tech. Univ. Hagenring, Braunschweig, D-38106, Germany
SOURCE: Angewandte Chemie, International Edition in English (1997), 36(5), 523-524
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:277316
GRAPHIC IMAGE:



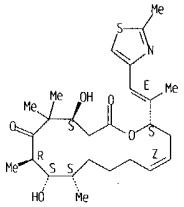
I II

ABSTRACT:
Stereoselective total synthesis of (-)-epothilone A and epothilone C was reported. The key step was the diastereoselective preparation of intermediate ketone I by an aldol condensation of II with (S)-2-methyl-6-heptenal.

IT 186692-73-9P, Epothilone C 186692-84-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (-)-epothilone A)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

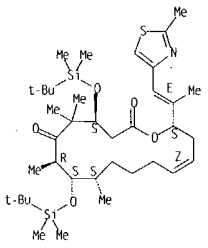
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 128 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

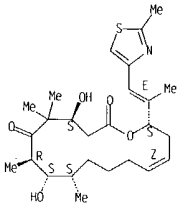
L5 ANSWER 129 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:175662 CAPLUS
DOCUMENT NUMBER: 126:225133
TITLE: Remote Effects in Macrolide Formation through Ring-Forming Olefin Metathesis: An Application to the Synthesis of Fully Active Epothilone Congeners
AUTHOR(S): Meng, Dongfang; Su, Dai-Shi; Balog, Aaron; Bertinato, Peter; Sorensen, Erik J.; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.
CORPORATE SOURCE: Laboratories for Bioorganic Chemistry and Biochemical Pharmacology, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Journal of the American Chemical Society (1997), 119(11), 2733-2734
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:225133
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
A ring closing olefin metathesis strategy for the synthesis of the previously encountered desoxyepothilone A (I) is described. A merging of the alkyl segment II (carbons 12-21) and acyl segment III (carbons 3-11) through an intermol. aldol-condensation reaction provided substrates needed for ring closing olefin metathesis. Thus, thiazole IV underwent olefin metathesis in C6H6 containing 50 mol % (PhCH:)[P(cyclohexyl)3]2RuCl2 to give 65% II and its E-isomer (Z:E 1:2). The results of these cyclization indicate a remarkable sensitivity to permutations of functionality at centers remote from the site of olefin metathesis. The in vitro biol. activity of E and Z desoxyepothilone as well as several related congeners is also described. I has IC50 range of 0.012-0.022 μM against drug-sensitive and -resistant human leukemic CCRF-CEM cell lines.

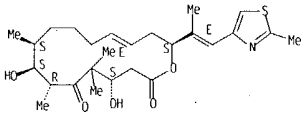
IT **188259-95-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antitumor epothilone congeners via ring-forming olefin metathesis)
RN 188259-95-2 CAPLUS

L5 ANSWER 129 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 188260-10-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

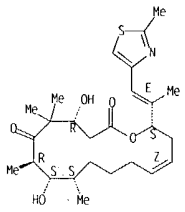


IT **188259-92-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antitumor epothilone congeners via ring-forming olefin metathesis)
RN 188259-92-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, [4R-[4R*,7R*,8S*,9S*,13Z,16S*(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 129 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4R,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

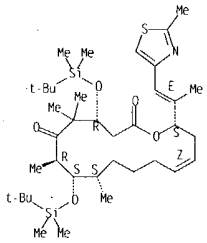
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **186692-73-9P**, (-)-Deoxyepothilone A **188260-10-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of antitumor epothilone congeners via ring-forming olefin metathesis)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

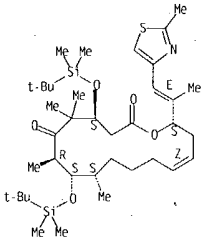
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

L5 ANSWER 129 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



IT **186692-84-2P 188260-22-2P 188260-30-2P**
188260-34-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of antitumor epothilone congeners via ring-forming olefin metathesis)
RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

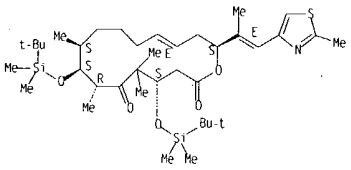
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-22-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-

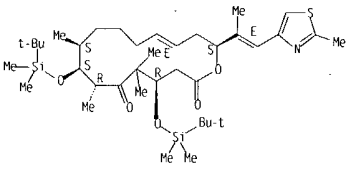
L5 ANSWER 129 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
dimechylethyl)dimethylsilyl]oxy]-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13E.16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 188260-30-2 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-bis[[(1.1-dimethylethyl)dimethylsilyl]oxy]-5.5.7.9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. [4R-[4R*.7R*.8S*.9S*.13E.16S*(E)]]- (9CI) (CA INDEX NAME)

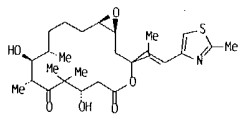
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



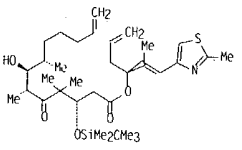
RN 188260-34-6 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4R.7R.8S.9S.13E.16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

L5 ANSWER 130 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:117381 CAPLUS
DOCUMENT NUMBER: 126:199371
TITLE: Total synthesis of epothilone A: the olefin metathesis approach
AUTHOR(S): Yang. Zhen: He. Yun: Vourloumis. Dionisios: Vallberg. Hans: Nicolaou. K. C.
CORPORATE SOURCE: Department Chemistry Skaggs Institute Chemical Biology. Scripps Research Institute. La Jolla. CA. 92037. USA
SOURCE: Angewandte Chemie. International Edition in English (1997). 36(1/2). 166-168
CODEN: ACIEAY: ISSN: 0570-0833
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:199371
GRAPHIC IMAGE:



I

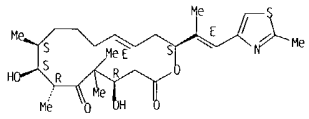


II

ABSTRACT:
The asym. total synthesis of epothilone A (I) from EtCOCMe2CHO. (S)-H2C:CH(CH2)3CHMeCHO and Et 2-methylthiazole-4-carboxylate via metathesis of olefin II is described.

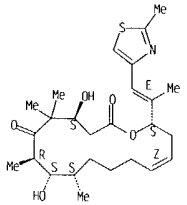
IT 186692-73-9P 187283-49-4P
RL: RCT (Reactant): SPN (Synthetic preparation): PREP (Preparation): RACT (Reactant or reagent)
(total synthesis of epothilone A via an olefin metathesis)
RN 186692-73-9 CAPLUS

L5 ANSWER 129 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



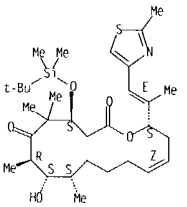
L5 ANSWER 130 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN Oxacyclohexadec-13-ene-2.6-dione. 4.8-dihydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13Z.16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 187283-49-4 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4-[[(1.1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-. (4S.7R.8S.9S.13Z.16S)- (9CI) (CA INDEX NAME)

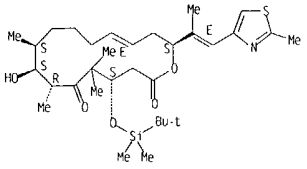
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT 187283-52-9P
RL: SPN (Synthetic preparation): PREP (Preparation)
(total synthesis of epothilone A via an olefin metathesis)
RN 187283-52-9 CAPLUS
CN Oxacyclohexadec-13-ene-2.6-dione. 4-[[(1.1-dimethylethyl)dimethylsilyl]oxy]-8-hydroxy-5.5.7.9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-

L5 ANSWER 130 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

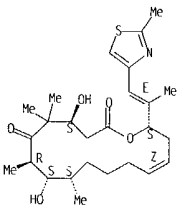
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

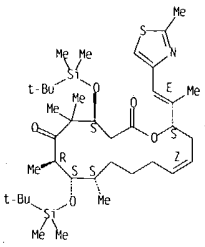
L5 ANSWER 131 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

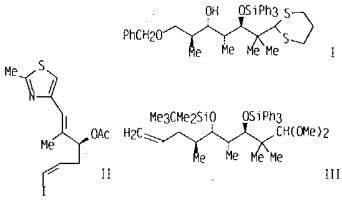
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 131 OF 131 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:72321 CAPLUS
DOCUMENT NUMBER: 126:144023
TITLE: Total synthesis of (-)-epothilone A
AUTHOR(S): Balog, Aaron; Meng, Dongfang; Kamenecka, Ted; Bertinato, Peter; Su, Dai-Shi; Sorensen, Erik J.; Danishefsky, Samuel J.
CORPORATE SOURCE: Lab. for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Angewandte Chemie, International Edition in English (1997), Volume Date 1996, 35(23/24), 2801-2803
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
GRAPHIC IMAGE:



ABSTRACT:
(-)-Epothilone A was prepared from dithiane I, (R)-glycidol and [(2-methyl-1,3-thiazol-4-yl)methyl]diphenylphosphine oxide via a B-alkyl Suzuki coupling of thiazole II with acetal III followed by closure of the macrocycle with an aldol reaction.

IT **186692-73-9P 186692-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (-)-epothilone A via a B-alkyl Suzuki coupling followed by closure of the macrocycle with an aldol reaction)
RN 186692-73-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-dihydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)-

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=> => s e4 or e6
           128 "AVERY MITCHELL A"/AU
             3 "AVERY MITCHELL ALLEN"/AU
L6         131 "AVERY MITCHELL A"/AU OR "AVERY MITCHELL ALLEN"/AU

=> s l6 and epothilones
           361 EPOTHILONES
L7           3 L6 AND EPOTHILONES

=> d 1-3 bib abs
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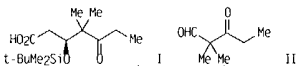
L7 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:106753 CAPLUS
DN 140:357086
TI Asymmetric aldol reactions using catalytic D-(+)-proline: a new, economic and practical approach to a commonly employed C1-C6 keto-acid synthon of the **epothilones**
AU Zheng, Yansong; **Avery, Mitchell A.**
CS Department of Medicinal Chemistry, University of Mississippi, University, MS, 38677, USA
SO Tetrahedron (2004), 60(9), 2091-2095
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier Science B.V.
DT Journal
LA English
GI



AB A new approach to keto-acid I, a common C1-C6 fragment used in the total synthesis of **epothilones** was initiated by direct aldol reaction of acetone with a pivaldehyde-like substance II, catalyzed with D-proline, leading to a 2,6-diketo alc. with better than 99% ee. Further intramol. closure of the diketone followed by oxidation of the silyl protected hydroxycyclohexenone led to the desired product I. None of the steps have been optimized, yet the overall yield for the four-step process is 31%. The use of com. available D-proline to construct the chiral center of I under very mild reaction conditions provided an economical and practical method for its construction.
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:184089 CAPLUS
TI Total synthesis of **epothilones** B and D amenable to large-scale preparation
AU Jung, Jae-Chul; Kache, Rajashaker; Vines, Kimberly; Zheng, Yan-Song; **Avery, Mitchell A.**
CS Medicinal Chemistry, University of Mississippi, University, MS, 38677, USA
SO Abstracts of Papers, 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003 (2003), MEDI-121 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69DSA4
DT Conference; Meeting Abstract
LA English
AB The novel structure and promising biol. activity of **Epothilones** A (1) and B (2), isolated and characterized by Hofle et. al. from myxobacterium Sorangium cellulosum, have evoked a great deal of interest. Along with their antifungal and microtubule-binding properties, these compds. have the advantage of better solubility than that of taxol, the ability to be obtained in multi-gram quantities, and increased potency over taxol multidrug-resistant cancer cell lines. A convergent and stereoselective total synthesis that is amenable to large-scale preparation of **Epothilones** B (2) and D (3) is described. The key steps are Normant reaction, Wadsworth-Emmons reaction of a Me ketone with a phosphonate reagent, diastereoselective aldol condensation of aldehyde with enolate to form the C6-C7 bond and macrolactonization.

L7 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:293388 CAPLUS
DN 136:325359
TI Methods of preparing **epothilones** and related analogs
IN **Avery, Mitchell A.**
PA The University of Mississippi, USA
SO PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002030356	A2	20020418	WO 2001-US32225	20011015
	WO 2002030356	A3	20040219		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002013248	A5	20020422	AU 2002-13248	20011015
	US 2002091269	A1	20020711	US 2001-981312	20011015
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to methods for preparing epothilone analogs, such as I and II [R1 - R4 = H, alkyl, alkenyl, alkynyl, (substituted) aryl, cycloalkyl, heterocycle; R5 = H, PMB, DPS, TBS; R7 = H, TBS, TROC, CO(CH2)4Me; R8 = H, TBS], via an aldol condensation of III or IV [R6 = H, TBS, TMSM PMBM, SEM], with V, VI or VII (M = alkali metal) to form condensation product followed by macrolactonization. Thus, epothilone B II (R1-R4 = Me; R7-R8 = H) was prepared via a multistep synthesis starting from (R,R)-α-methyl-oxiranemethanol, 1-bromo-4-methyl-4-pentene, propyne and di-Et [(2-methylthiazol-4-yl)methane]phosphonate. The present invention also provides chemical compds., and methods for producing such chemical compds., that are useful in producing I and II.

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